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THE LOBULES OF THE MAMMALIAN CEREBELLUM AND CEREBELLAR NOMENCLATURE*

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The presentation of this general subject, made in the paper [1] previously published in the ARCHIVES, concerned itself chiefly with a detailed description of the mammalian cerebellum from the point of view of the arbor vitae and the folial pattern. This second study endeavors to carry somewhat further the direct comparison of the various subdivisions of the mammalian cerebellum by taking up each lobulus from the same points of view and drawing such conclusions as may seem warranted. This approach renders possible the attempt to establish direct homologies between the discrete subdivisions of the mammalian and the human cerebellum. In carrying out this investigation the chief difficulty encountered was the overloaded and confused state in which cerebellar nomenclature has enmeshed itself, and not the least purpose of this paper is to attempt to rid the cerebellum of this encumbrance and to substitute a more rational and descriptive terminology, discarding the old fantastic and symbolic terms.

HOMOLOGIES IN CEREBELLAR STRUCTURE

If the evolutional expansion of the cerebellum is viewed as a whole and the special claims of particular parts are made subservient to the entire picture, a comparative study of the organ indicates a relatively orderly progress of development. In all comparative anatomic studies, however, forms can be discovered which by reason of some inherent impetus or of some environmental influence have gone on their own individual course to degrees of morphologic specialization that have profoundly modified their phylogenetic endowment. Such examples can readily be found in this series and are exemplified by the sloth and the aquatic forms. In the former, motor organization to a large

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extent has been suppressed, an almost static condition of existence has been reached, and the cerebellum directly reflects this modification in its much simplified structure. In the water-living forms, such as the aquatic carnivores, the sirenia and the cetacea, an enormous modification in somatic development has taken place, and this change in motor organization is clearly manifested in the equally metamorphosed cerebella of these forms. A similar but much more restrained transformation is shown in the beaver, the cerebellum of which is markedly different from the other rodents, particularly in the unusual development of the proximal portion of the paraflocculus. Those who are familiar with the natatorial capabilities of the beaver will recognize the perfection of his adaptation to an aquatic environment. The beaver, however, has retained his quadrupedal equipment and perhaps this persistence of the locomotor apparatus has militated against the extreme modification of the cerebellum shown in other water-living forms. The majority of the animals, however, have remained more or less closely approximated to the central stem of quadrupedal organization and show considerable fixity in cerebellar development. In all of them it is not difficult to draw homologies between the various subdivisions of the cerebellum and the fissures which serve as surface differentiations between homologous units.

The fundamental principle which must be accepted at the outset in any attempt to understand and homologize the various parts of the cerebellum is that this part of the brain is an organ which develops along axial lines, that it has a cephalic and caudal extremity and that the tissue intervening between these two extremities has undergone a series of complicated modifications chief among which is the relative increase in its bulk. Every morphologic investigator of the cerebellum has early acknowledged the necessity of viewing the organ in this light, and all cerebellar schemas are predicated on a study of the entire structure spread out in one plane, thus reestablishing the primitive anatomic relationships and removing the difficulties and apparent contradictions which its adaptation to spatial requirements has necessitated. The first result of this conception of the cerebellum is to remove the great importance which has been attached to the sulcus horizontalis magnus almost solely through its fortuitous anatomic situation. This sulcus represents the transition from the cephalic to the caudal aspect of the organ. It is a sulcus of very recent phylogenetic importance since it attains its special recognition only late in the developmental scale, namely, in the anthropoid apes, making its appearance as such first in *Simia satyrus*, the orang-utang, and increasing as the bulk of the cerebellum expands through the gorilla, chimpanzee and man. Embryologically, it appears relatively late, in the middle of the fourth month of fetal life, considerably after the appearance of the primary fissure and

somewhat later than a number of the other fissures. Morphologically, it is inconstant, and its transition across the midline to meet its fellow of the opposite side is often incomplete. From studying the comparative morphology of the mammalian cerebellum, it would seem to be the homolog of the sulcus intercruralis, which is a by-product of the arrangement of the two crura of the lobulus ansiformis through the approximation of the mesial extremities of the folia of crus 1 to the same structures of crus 2. In human morphology, the sulcus horizontalis magnus divides the cerebellum into a dorsal and a ventral half, a differentiation which may have its advantages in cadaveric descriptive anatomy, but serves no useful purpose whatsoever in the attempt to understand the philosophy of the cerebellum and results only in confusing the picture by producing an entirely artificial division of lobulus C. This lobulus shows the clearest evidence of evolutional development in response to the needs of the body economy, reflects the enormous influence of the superposed cerebrum on its morphology and should not be arbitrarily split up unless this division can be based on physiologic

Fig. 1.—The constitution of the middle lobe, according to (*A*) Henle, (*B*) Schwalbe and (*C*) Kuithan. From Bolk.

grounds. This lobulus expands progressively under the increasing contribution of the pallium to the organization of cerebellar function, and an artificial subdivision such as this serves merely as an impediment. It can therefore be seen that the primary division of the cerebellum into a dorsal and a ventral half by the great horizontal fissure is a purely arbitrary and irrational procedure, that it has no basis in embryology, phylogeny or physiology, and that its only claim to continued existence depends on its adventitious morphologic position.

The division of the cerebellum by the fissura primaria and the ventricular fastigium into a cephalic and a caudal lobe is accepted by all comparative morphologists. This partition of the cerebellum is so well defined in all the cerebella examined, excluding only the cetacea, so constant in its relative position and so early in its appearance embryologically that all have adopted this evident morphologic differentiation. Only irrefutable evidence of functional localization remains lacking to add the confirmation of physiology to the weight of evidence in favor of this fundamental separation. The second well defined and constant sulcus, both morphologically and embryologically, is the fissura secunda

which separates the paraflocculär and flocculär portions of the cerebellum from the more cephalic part of the caudal lobe.

Many investigators have seemed to be impelled to divide the cerebellum into three lobes, a cephalic, a middle and a caudal lobe. To establish these divisions the fissura primaria and the fissura secunda would seem to present inviting boundaries for the three subdivisions, but their rather obvious claims have been ignored and a number of artificial differentiations have been attempted. The most logical arrangement would place the cephalic lobe rostrad to the fissura primaria, the caudal lobe caudad to the fissura secunda and the middle lobe between these two fissures. These natural lines of cleavage have not been followed, and in the formulation of the three lobes much diversity of opinion has manifested itself.

Fig. 2.—Cerebellar schema according to Ingvar. The middle lobe is indicated by dots and consists of the so-called lobulus simplex and the vermal portion of lobulus C 2. *1* represents the cerebellum of a crocodile, *2* that of a bird; *3*, that of mammals.

Henle, followed by Dejerine, included in the middle lobe only a part of what may be schematically referred to as lobulus C 2, excluding the more cephalic two medullary rays from its composition. Schwalbe extended the middle lobe to include the remainder of C 2 by advancing the cephalic limit of the lobe to the fissura primaria. Kuithan, on the other hand, included in his middle lobe the cephalic two thirds of lobulus C 2. To render the situation even more confused, Ingvar illustrated the middle lobe as having an apparently compound constitution, its cephalic portion being represented by the lobulus simplex extending across the entire dorsal surface of the cerebellum, whereas its caudal part is confined to the vermis and comprises the entire vermal representation of lobulus C 2 without including the lateral derivatives of lobulus C 2, crus 1 and crus 2. This gives the middle lobe of Ingvar a constitution which cannot be defended from comparative anatomic or embryologic points of view.

Recently, Mussen endeavored to establish the constitution of the middle lobe on the basis of the response obtained from the somatic musculature by subcortical electric excitation of the cerebellum. Stimulating as these experimental results are and will be to the study of cerebellar localization, it would seem that the delimitation of anatomic unities by means of physiologic experimentation, which must be confirmed time and time again before being finally accepted, is somewhat hazardous, particularly as these delimited areas do not entirely conform to homologous entities. The standing of the middle lobe is therefore distinctly compromised by this failure of unanimity of opinion. If any division of the cerebellum on morphologic lines into these lobes

Fig. 3.—Lobulus 1 arbor vitae.

is considered advisable, it would seem a more defensible position to include the entire region between the fissura primaria and the fissura secunda as the middle lobe. Apparently no desirable end can be attained by such a further subdivision of the caudal lobe and it is perhaps advisable to discard the conception of a middle lobe in this sense. It should be our purpose to simplify and not to render more incomprehensible the difficult morphology of the cerebellum.

The division of the arbor vitae depends on the development of the medullary rays which arise from the central core of the white matter and radiate toward the periphery. These stems are relatively constant, the only chief variant in the cephalic lobe being ray 3 which occurs frequently enough to enforce its occasional independent existence and requires recognition. This shoot presents a very considerable degree

of variation; when its independent origin from the medullary center has been lost, it usually is incorporated in ray 4 as a cephalic branch which is then called ray 4 A.

In this analysis of the lobules of the cerebellum the anatomic homologies between the mammalian and the human cerebellum can be traced. At the same time some attempt may be made to carry forward the tentative conclusions reached in the more general description which was published a year ago. As was mentioned in that paper, certain ascriptions of function have been made to the various subdivisions of the cerebellum by those who have labored in this field, namely Bolk,

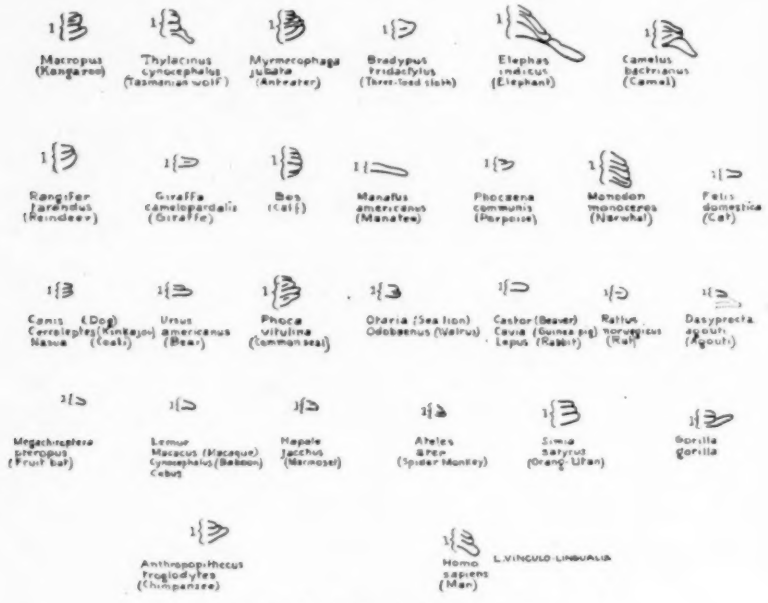


Fig. 4.—Lobulus 1 folial pattern.

André Thomas, Durupt, Van Rijnberk and others. It was the hope in this comparative study that some new material might be discovered which would throw light on this interesting aspect of the problem.

In considering the accompanying illustrations, one factor must be borne in mind, namely, that in drawing the figures no account could be taken of the many folia that are submerged in the fissures which limit the lobules. The figures represent the lobules as they are seen on the surface of the intact cerebellum. Except where the hemispheral components greatly exceed the vermal representations, some idea of the submerged folia may be obtained from a study of the transsected folia as they appear in the representation of the arbor vitae.

When more than one name is placed below the drawing of any lobulus, the form of the lobuli is so similar that one type represents all of the individual animals.

In the great majority of instances ray 1 can be readily distinguished, and it with its cortical envelope makes up the first lobule. The lobule can be traced through many modifications throughout the mammalian series to man. Its modifications are chiefly concerned with the actual mode of origin from the central white matter. In the majority of instances it arises as a definite shoot, while in others the ray is merged with the supporting superior medullary velum and is not clearly evident.

Fig. 5.—Lobulus 2 arbor vitae.

This mode of formation appears in man and for this reason it is called the lingula, "a little tongue." The detailed form is not of great importance; the lobule is usually distinct and its comparative anatomy is not difficult to recognize. It usually does not present any extension into the hemisphere but occasionally small lateral outgrowths are seen.

According to the formal schematization, the first lobulus is supposed to preside over the synergic association of the eye muscles. To extract any confirmation of this view from this comparative representation is impossible. As has already been pointed out, the eye movements in the great majority of these forms are relatively rudimentary; in many the question of any extensive conjugation of eye movements is almost eliminated by the fact that the eyes are situated in such a position that there is no or very little overlapping of the visual fields

and therefore but little opportunity for conjugated movement. In those forms in which the eyes are so placed as to allow any wide latitude of movement and any extensive development of conjugate gaze, as in the anthropoid apes and in man, the increase of cerebellar tissue to provide for such synergy is not to be found.

There is to be derived, therefore, no confirmation of the functional localization of ocular synergia from this comparative morphologic study, and the definite identification of the physiology of this part of the cerebellum must depend on other methods of investigation.

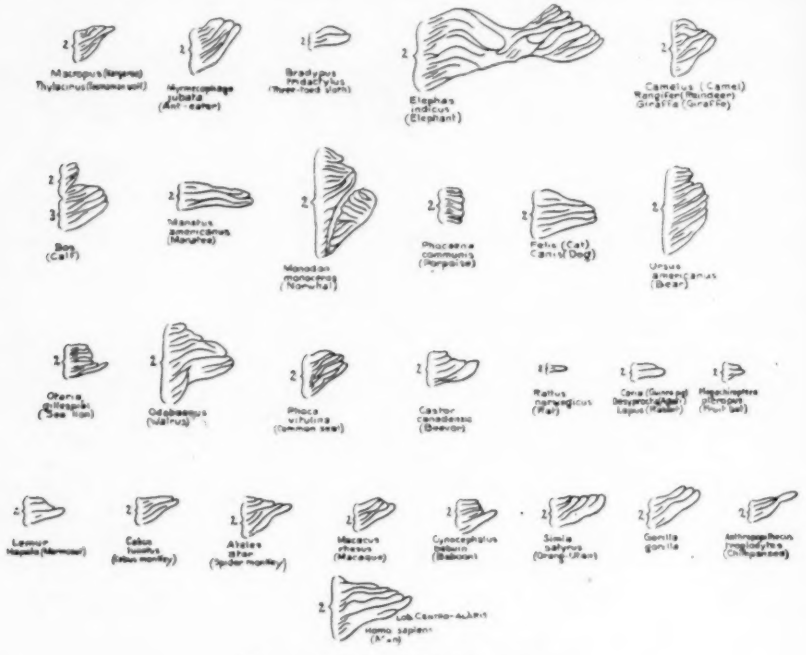


Fig. 6.—Lobulus 2 folial pattern.

The second medullary ray, with its folia, is single only in the simplest of the cerebella and in some of the primate forms. In the remainder the ray is usually represented by from two to four shoots which form a not inconsiderable portion of the cephalic lobe. In man the lobulus is called the lobulus centralis. Its composition is relatively easy to establish and the maintenance of its identity through the series can readily be determined.

The lateral extensions of lobulus 2 extend outward into the hemisphere as thin laminae which are disposed parallel to one another and present no complications in the orthodox cerebella. Lobulus 2 lateralis is demarcated from lobulus 1 lateralis and also from lobulus 4 lateralis

by clearly defined lines of separation in the continuance outward of the fissures which separate these two structures in the arbor vitae.

According to physiologic investigators, lobulus 2 presides over the synergic movements of the tongue. Of the forms examined, the outstanding individuals in so far as their lingual equipment is concerned are *Mymecophaga jubata,* the ungulates and the primates. The anteater possesses a tongue which is in some instances 6 or 8 inches in length, can be extended from the mouth almost to its extreme limit and can be dexterously used in lapping up the food on which the animal subsists, and yet lobulus 2 is no larger in the anteater than it is in the kangaroo or the seal. In the primate series, no marked contrast in bulk or complexity can be found in man, in whom the synergic

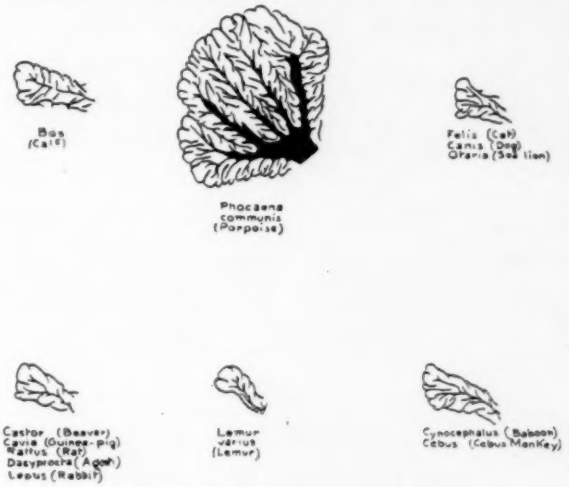


Fig. 7.—Lobulus 3 arbor vitae.

manipulations of the tongue have reached the acme of perfection in the modulation of the spoken and singing voice and the interaction of the tongue, lips, jaws and larynx. No such allocation of function would support the contrast between lobulus 2 of the bear and the other carnivores in which the former greatly surpasses the latter. It would therefore appear that this study does not lend any degree of support to this localization.

The extreme degree of variability manifested by lobulus 3 would at once cast doubt on any attempt to localize function in this lobule. Lobulus 3, as it is recognized in this presentation, appears with constancy as an independent lobulus only in the rodents. It would seem that the independent existence of lobulus 3 does not depend on any particular quality of motor organization but rather on some vagary of morphologic development, and therefore the ascription of any definite

function to it would seem indefensible. The sketchy morphologic history of lobulus 3 suggests no compelling physiologic differentiation within this lobulus and by no stretch of the imagination can any support be obtained for the contention that it controls the masticatory apparatus.

Lobulus 4 vermalis is formed by the fourth medullary ray and its investment of gray matter. The spray of white matter is usually double its cephalic shoot representing, in the majority of instances, the ray which in some forms attains independence and is called ray 3.

The folia of lobulus 4 vermalis are continued outward as parallel strips of gray matter supported by the central white core. They may be subdivided into two compact groups in accordance with the division of ray 4 into ray 4 A and B. This separation, however, does not penetrate deeply into lobulus 4 lateralis and the folia are not dispersed.

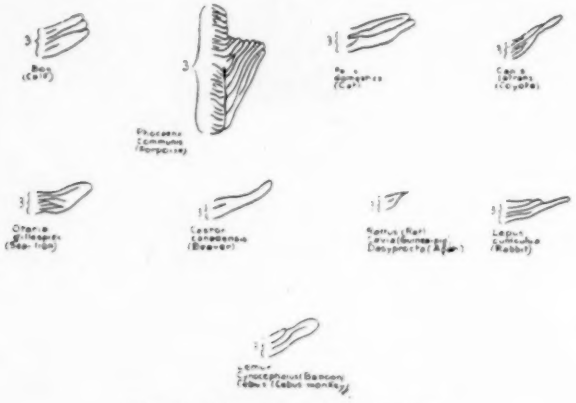


Fig. 8.—Lobulus 3 folial pattern.

This lobulus is clearly homologous with those in a similar position in the mammalian series. The caudal limit of lobulus 4 is the fissura primaria.

The claim that lobulus 4 presides over the synergic integration of the mimetic musculature and the activity of the lingual and pharyngeal muscles can acquire but little support from this exposition of the comparative constitution of this lobule. So far as the mimetic musculature is concerned, this is practically nonexistent except in the carnivores and primates. The lingual and the pharyngeal musculature would seem to be about equal in their demands in all the forms except on the basis of the actual number of muscles and the mass of such muscles that must be synergized. The particular demands, so far as the mimicry, phonation or deglutition which the elephant and the narwhal can advance, would not seem to account for the relatively large size and complicated form of this lobule in these animals. The steady advance of this

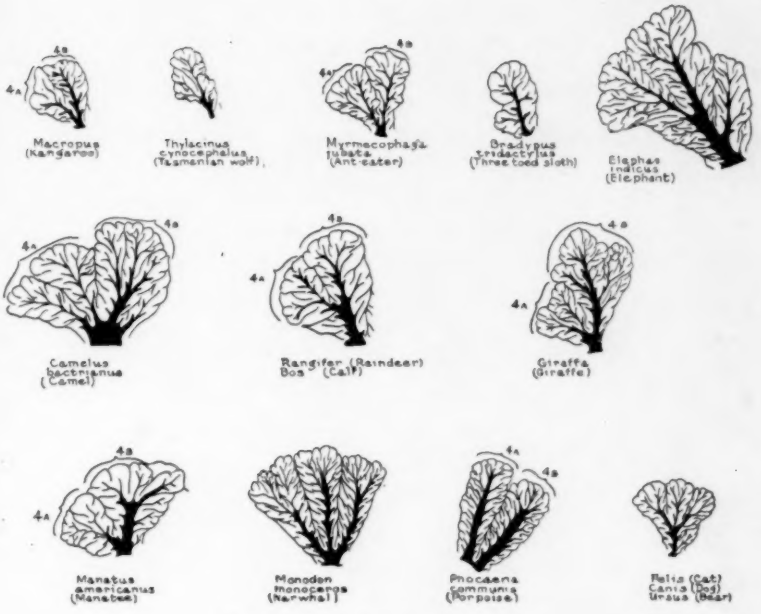


Fig. 9.—Lobulus 4 arbor vitae.

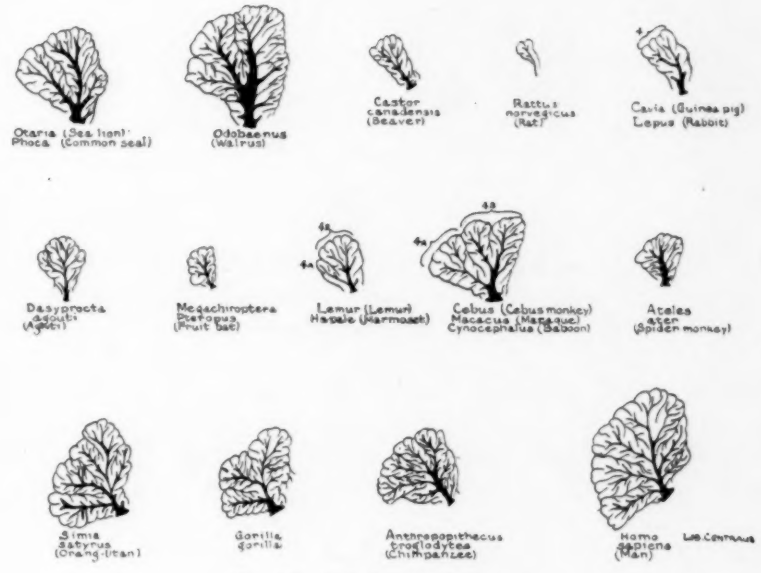


Fig. 10.—Lobulus 4 arbor vitae.

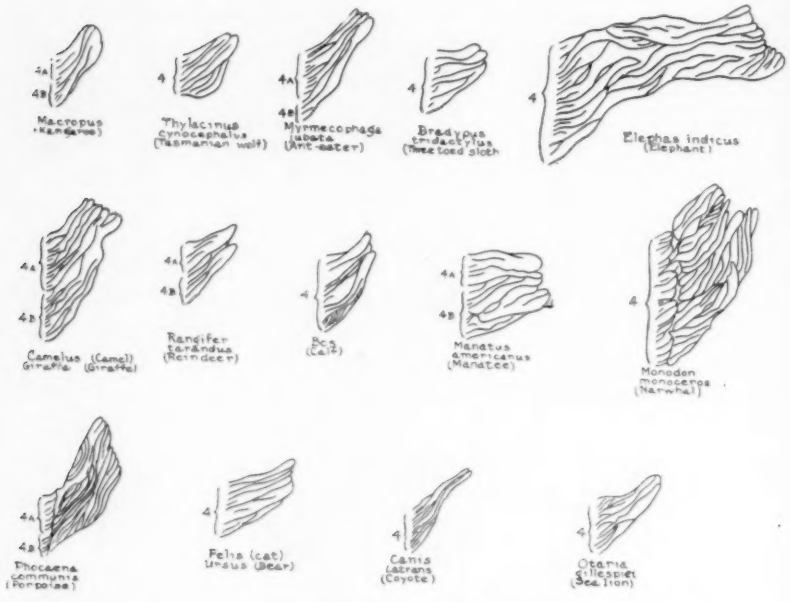


Fig. 11.—Lobulus 4 folial pattern.

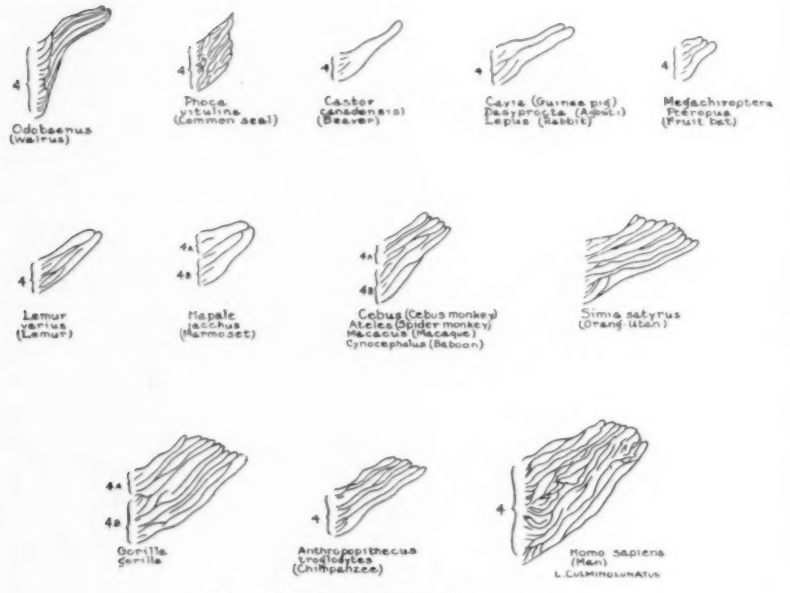


Fig. 12.—Lobulus 4 folial pattern.

lobulus through the primates to man may lay some basis for this functional localization, but the whole mammalian order supplies no substantiation for this view.

A more complicated situation exists in the caudal lobe. The fundamental division of the lobe into three lobules, C, B and A, was easily followed in the majority of the cerebella examined. Lobulus C 2 is usually subdivided into lobuli C 2 and C 1. In man, lobulus C 2 has been subdivided into three minor lobules through the extreme differentiation of its lateral extensions. The names attached to these three subdivisions of lobulus C 2 are the clivus, the folium cacuminis and the

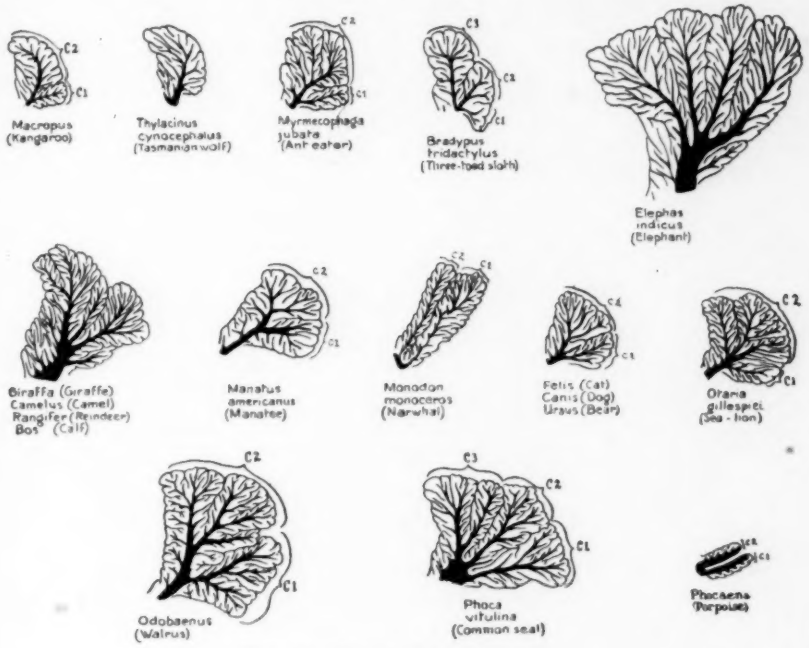


Fig. 13.—Lobulus C arbor vitae.

tuber valvulae. This designation of three subsidiary lobules does not find any real justification in the form of the human arbor vitae which can be readily homologized with lobulus C 2 vermalis of the mammalian series. Consequent, however, on the enormous expansion which has resulted from the inpouring of neuraxes from the palliopontocerebellar system, the lateral portion of lobulus C2 has undergone an extraordinary differentiation in man. The orderly course of this process can be readily traced in the primate series. In the lower forms, those possessing a lissencephalic type of cortex and a small middle cerebellar peduncle, is found the typical quadrupedal type of cerebellar organization. As mammalian differentiation proceeds and as the pallium

becomes more and more gyrencephalic, ever-increasing contributions from suprasegmental sources pour into this portion of the organ and it becomes the dominating region of the human cerebellum. Its cephalic demarcation is easy to determine, being the fissura primaria, but its caudal line of separation from the lateral extensions of lobulus C 1 is somewhat more difficult. If the fissura primaria and the fissure separating lobulus C 2 from lobulus C 1 are carefully followed, the lateral mass of lobulus C 2 can be readily isolated. This mass of folia therefore corresponds to the lobulus ansiformis with its two crura separated from each other by the sulcus intercruralis. If the lateral lobule be further investigated, it will be found to be divided into two roughly

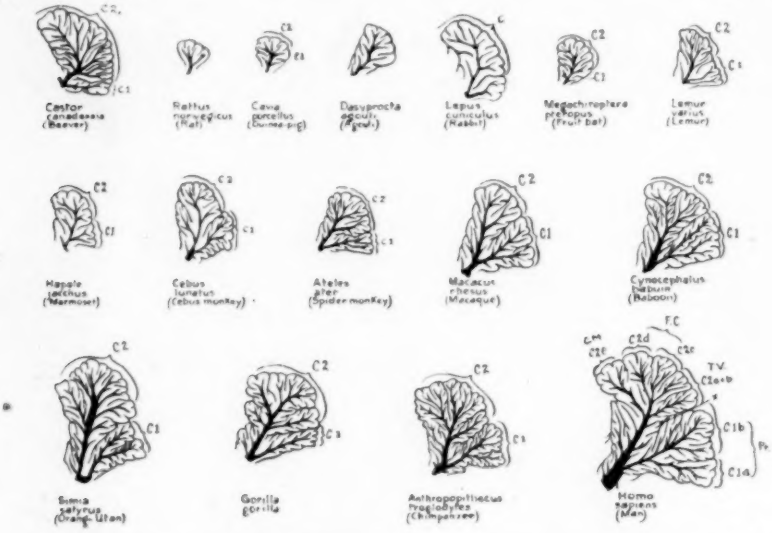


Fig. 14.—Lobulus C arbor vitae. In the representation of the human lobulus *C 2, C. M.* represents culmen monticulus, *F. C.* folium cacuminis, *T. V.* tuber valvulae and *C 1, Pr.* pyramis.

equal halves, cephalic and caudal, by the great horizontal fissure. If the edges of this fissure are separated, the folia which end in it will be found to present their mesial extremities toward one another while their lateral extremities proceed toward the periphery of the lobule. This is essentially the arrangement that is found in the composition of the sulcus intercruralis, and these two fissures would appear to be one and the same. The lateral folia cephalad to the great horizontal fissure are, therefore, the homologs of those forming crus 1 and the lobulus simplex. In human morphology they are called the lobulus lunatus posterjor, connected with the clivus mesially, and the lobulus posterosuperior, the lateral continuation of the folium cacuminis. The remainder

of the lobulus, caudal to the great horizontal fissure and cephalad to lobulus C 1, therefore becomes homologous to crus 2, and the folia are found to arrange themselves as do the simple folia in the lower forms, namely, in a gradually shortening chain of lamellae the proximal ends of which terminate in the fissure. These folia are connected to the tuber valvulae and form, cephalo-caudad, the lobulus postero-inferior, the lobulus gracilis posterior and the lobulus gracilis anterior.

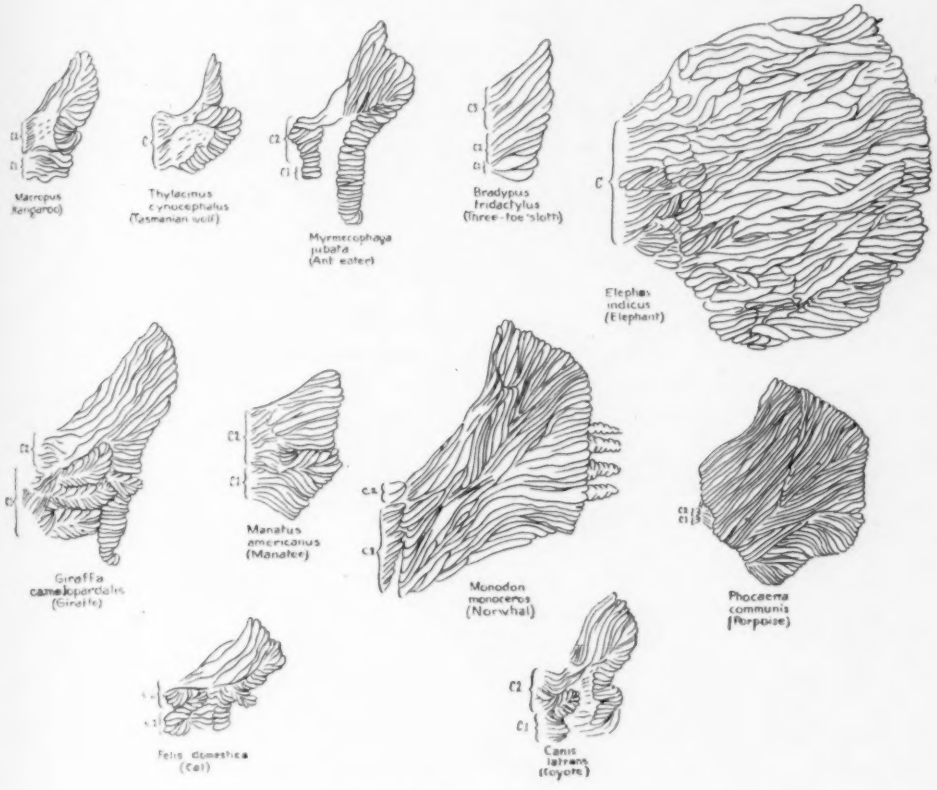


Fig. 15.—Lobulus C folial pattern.

The smaller caudal portion of lobulus C is formed by the medullary stem C 1 which acts as a supporting structure for lobulus C 1. This subdivision has also been easily followed through the series, although in some forms its importance has been subject to considerable subsidence and it has been recognizable only as a submerged folium. Its great morphologic significance, however, has been in its evidence as to the identity of its lateral extensions forming the lobulus paramedianus, for in some of the primitive cerebella the folia have extended outward

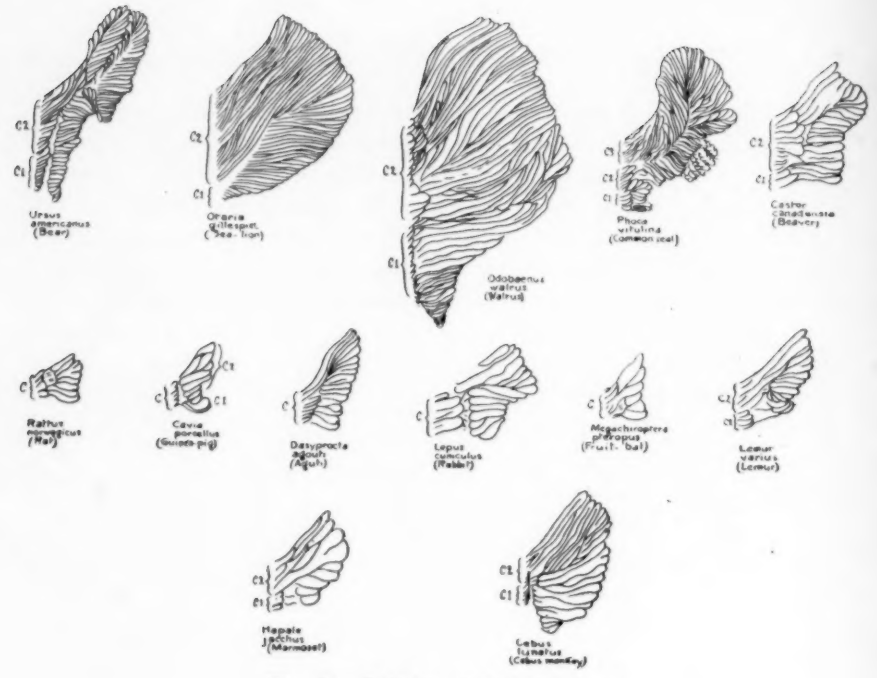
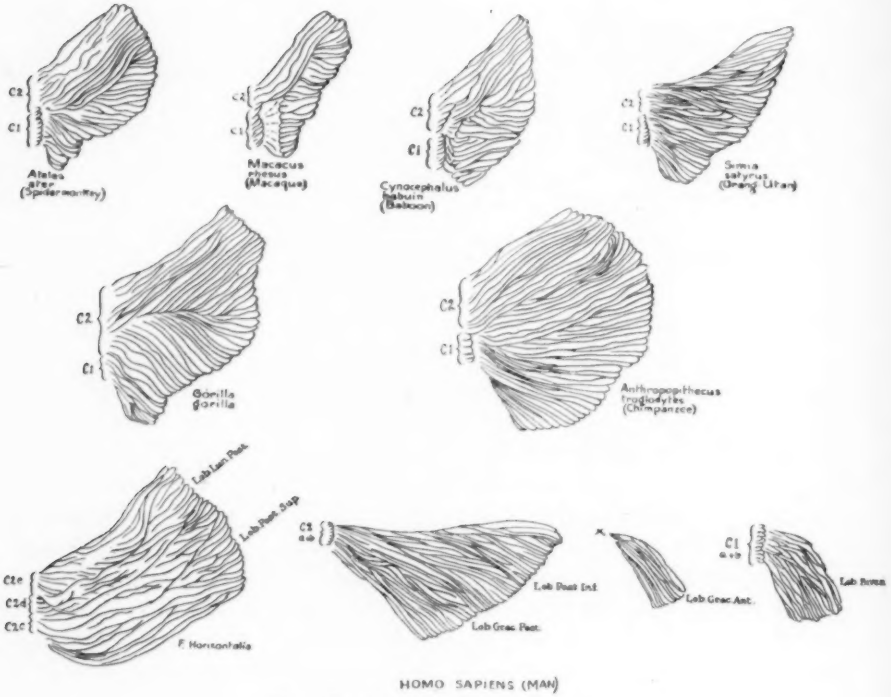


Fig. 16.—Lobulus C folial pattern.



HOMO SAPIENS (MAN)

Fig. 17.—Lobulus C folial pattern.

uninterruptedly into the lateral chain and thus establish the unity of the vermal and lateral folia. This lobulus in human anatomy is called the pyramis, meaning a "pyramid," with perhaps some contoural justification. This lobulus is separated from lobulus C 2 by a secondary fissure and from the succeeding lobulus B by the fissura secunda which is second only in constancy and prominence to the fissura primaria.

The separation between lobuli C 2 and C 1 is definite, although in man the infolding which a little more caudally will produce the so-called tonsil is beginning to confuse the picture. The caudal line of demarcation of lobulus C 1 is of considerable importance, for in the mammalian series the fissura secunda differentiates the formatio vermicularis or the parafloccular formation from the more cephalic part of the caudal lobe of the cerebellum. The lateral extensions of lobulus C 1 can, however, be traced into that part of the human cerebellum which is called the lobulus biventer. The folia forming the lobulus biventer, therefore, correspond to those forming the lobulus paramedianus of the comparative cerebellum. These folia rapidly shorten in lateral extent and become so displaced by the infolding process as to lie at right angles to the course of the majority of the cerebellar folia, with their axes in a cephalocaudal direction. The caudal folia of the lobulus biventer give place to the next succeeding part of the lateral hemisphere, the tonsil.

Lobulus C presents a variety of form which defies any attempt at offhand diagnosis as to functional localization. It, with the paraflocculus, presents evidence in certain groups of the mammalian order which would seem to bear the stamp of authenticity in regard to functional localization. The orderly progressive expansion in this part of the primate cerebellum depends directly on the contribution of the pallium to the cerebellum through the palliopontocerebellar pathways and the inferior olivary complex. When this anatomic fact is considered in connection with the activities of the forms which manifest this increase, there can be but little doubt that the explanation for this local augmentation in size is accounted for by the integration of the muscles in the production of the skilled acts, particularly those of the upper extremity, the hands and the fingers. It is difficult on this basis, however, to explain the sporadic expansions in this lobulus which are met with in the aquatic forms. In these animals there is but little motor differentiation in the fore limbs, and especially in the distal segments. Some other influences must be active in this regional development which are not apparent at the present time. One specialization which is of more than passing interest is the peculiar form of the lobulus in the bear, in which a definite reduplication of the lobulus is apparent and is unique in the series. The significance of this variation is not evident.

Lobulus B and its lateral extensions forming the formatio vermicularis of Bolk have undergone greater transformation than any other part of the cerebellum. These modifications may easily be appreciated by a glance at the comparative history of this part of the cerebellum. It has varied from a tiny roset of three or four folia in the rodents and the bats to a structure forming three fifths of the entire mass of the cerebellum in the cetacea. Its form and contour have also been profoundly modified in the various forms examined. The lateral extensions are either in direct continuity with the vermal folia or may be widely separated from them. In the latter instances, however, more

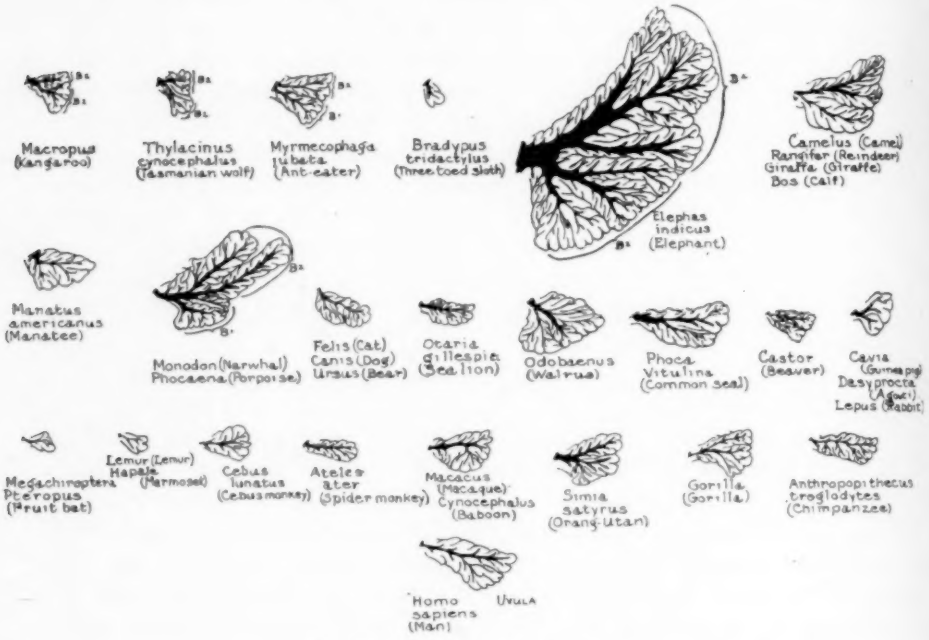


Fig. 18.—Lobulus B arbor vitae.

or less well defined ridges on the surface of the medullary core may be found, indicating the underlying union between lobulus B and the formatio vermicularis. In its devious history numerous modifications appear which have resulted in the separate designation of its parts as the crus ascendens, the lobulus petrosus, the paraflocculus, the crus descendens and its termination, the uncus terminalis. If these distractions be ignored, the entire structure may be termed the lobulus paraflocculus. In man, lobulus B is called the uvula, and its hemispheral moiety, the tonsil. The identifying criteria which homologize these structures are the fissura secunda and the faintly discernible connections between the vermal and hemispheral constituents.

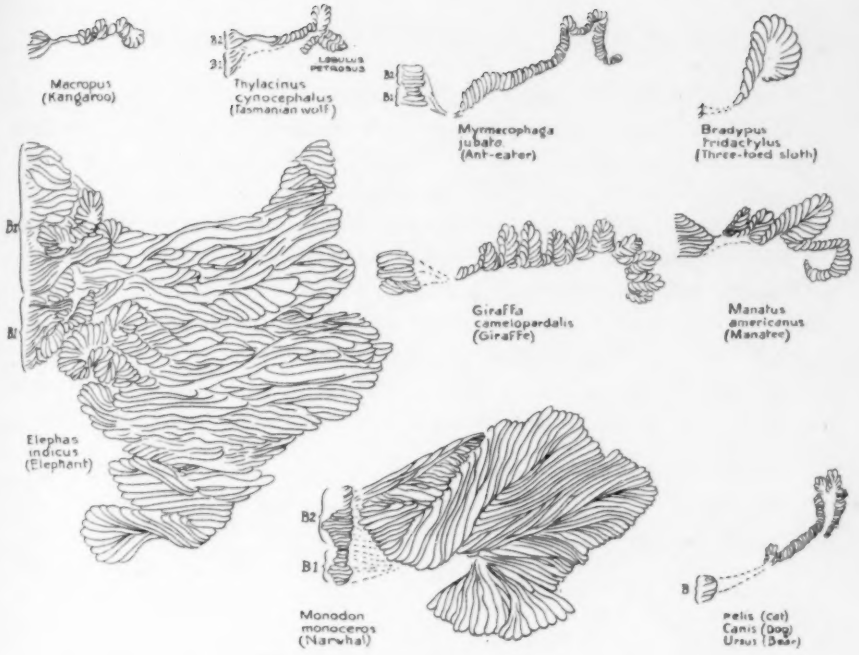


Fig. 19.—Lobulus B folial pattern.

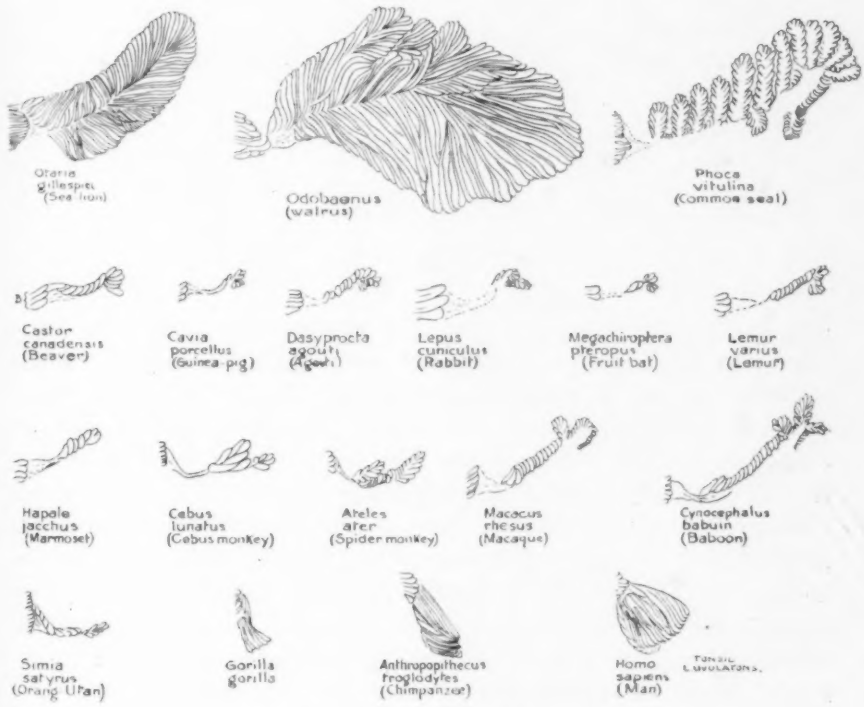


Fig. 20.—Lobulus B folial pattern.

Lobulus B with its lateral portion forms the formatio vermicularis or the paraflocculus. In most of the examples it presents a rather evident fixity of pattern and development which would stamp it as being a somewhat subservient but relatively constant portion of the cerebellum and as such contributing a similar function in all forms. In certain individuals, however, the paraflocculus undergoes an enormous expansion, and from the fact that this sudden emergence into prominence of this part of the cerebellum appears in forms with a uniform habitat, although belonging to separate classes or orders, would seem to have definite significance. The vermal portion of the cerebellum does not seem to be implicated to the same extent as is the hemispheral divi-

Fig. 21.—Lobulus A arbor vitae.

sion, and maintains a fair degree of constancy in its make-up except when bulk enters into consideration. The elephant, of course, provides the chief example of the latter phase of the subject, both in the arbor vitae and in the folial pattern. The group which shows the predominant development of the paraflocculus is that which includes the water-living forms. These are the sirenia, the cetacea, the aquatic carnivores and *Castor* (the beaver) among the rodents. This specialization of function and its correlation apparently rests on the assumption that the paraflocculus provides the region in which the synergic associations of the axial and appendicular musculature takes place. The conjunction of an aquatic habitat with a predominant parafloccular development provides at least a fair support for this presumptive functional localization.

The last medullary outgrowth forms ray A and constitutes a comparatively little modified lobulus A. In human morphology it is called the nodulus, and its lateral constituents, by some strange chance of fortune, are called the flocculus both in man and in the subhuman members of the mammalian order. As with the preceding subdivision of the cerebellum this union is not direct but can be traced over the medullary core, the lateral portion being displaced to a considerable distance

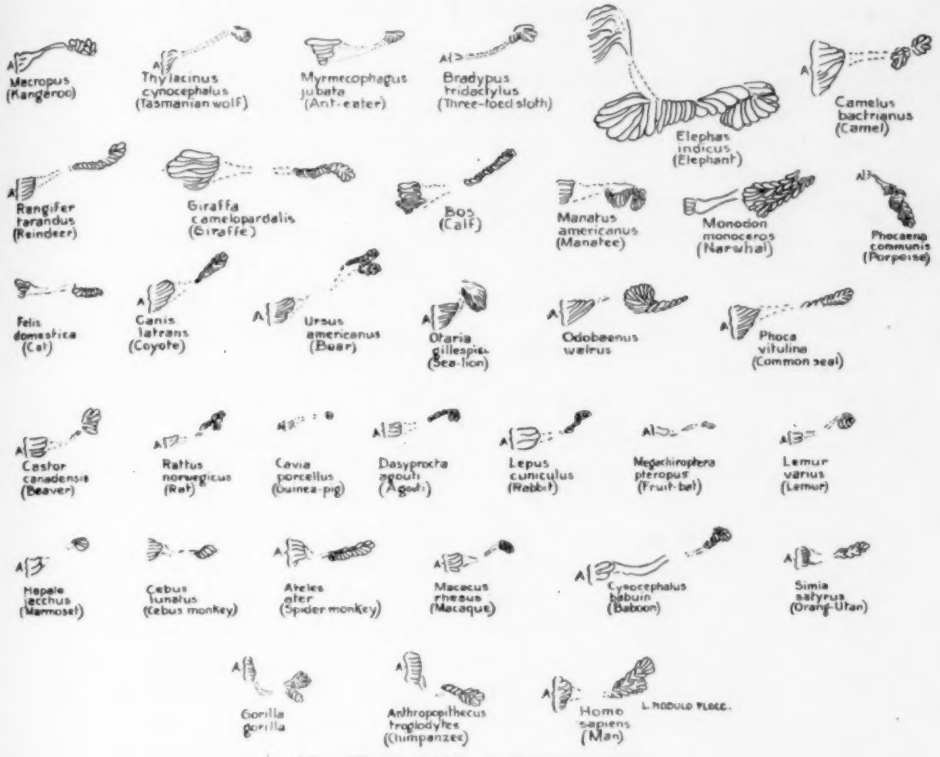


Fig. 22.—Lobulus A folial pattern

from the vermal part, although embryologically they are derived from a united subdivision of the cerebellum.

The variations in the development of lobulus A and the flocculus provide no definite material for the assumption of functional localization.

These homologies would seem to be definite and offer no evidently insuperable obstacles. The establishment of such homologies would indicate that the cerebellum throughout the entire mammalian order develops along similar lines and that in general the same principles, varying, however, in degree, influence the development of its final form.

The cephalic and caudal constituents of the cerebellum present but little modification. They are relatively unvarying in the mammalian class; the process of evolution and the response to functional demands are complied with by the more plastic intermediate portions of the cerebellum. Except for the aquatic forms the parafloccus seems to demonstrate this same tendency to inflexibility of morphologic structure, and lobulus 2 does not offer much more material for conjecture. Lobulus 4 and lobulus C are the varying constituents of the cerebellum. In lobulus C certain definite influences can be seen to play important rôles.

It would seem manifest that this comparative morphologic approach has brought to light some evidence which, if used in a collateral way, may be of considerable advantage, but the knowledge gained from this sort of study will not go far toward unraveling the intimate intricacies of cerebellar function. The ultimate elucidation of cerebellar physiology must depend, in the last analysis, on careful experimentation and the comparison of localized lesions with disturbed cerebellar function.

The great importance of these homologies at the present time lies in their evident applicability to the problem of simplifying cerebellar nomenclature.

CEREBELLAR NOMENCLATURE

The confused situation in which the anatomist finds himself when he is faced with the complications of cerebellar nomenclature cannot be equaled by any other part of the nervous system except the rhinencephalon. There can be but little argument that the greatest and most oppressive difficulties that have been added by successive generations of anatomists to an appreciation and understanding of the morphology of the brain by physicians and students have their existence in the fantastic and bewildering intricacies of descriptive terminology. This process reached its culmination in the efforts of anatomists to differentiate the various subdivisions of two parts of the nervous system, the rhinencephalon and the cerebellum. With the former, this zeal can be dismissed with scant mention on account of the fact that the story of the rhinencephalon belongs definitely to the limbo of the past. It represents the ten-times-twice-told tale of the cerebrum and bears but little relationship to the pressing problems of the present. The cerebellum, however, stands in a different relationship to present-day study and investigation. It is an organ which plays a vital rôle in present-day symptomatology and is still the object of careful, painstaking, scientific investigation. It is a part of the brain the function of which is still not definitely established, and the physiology of its activity and the actual neuronal connections established by its many categories of morphologic entities remain still a matter of controversy and conjecture. At least one of the objects of cerebellar investigation should be the elimination of

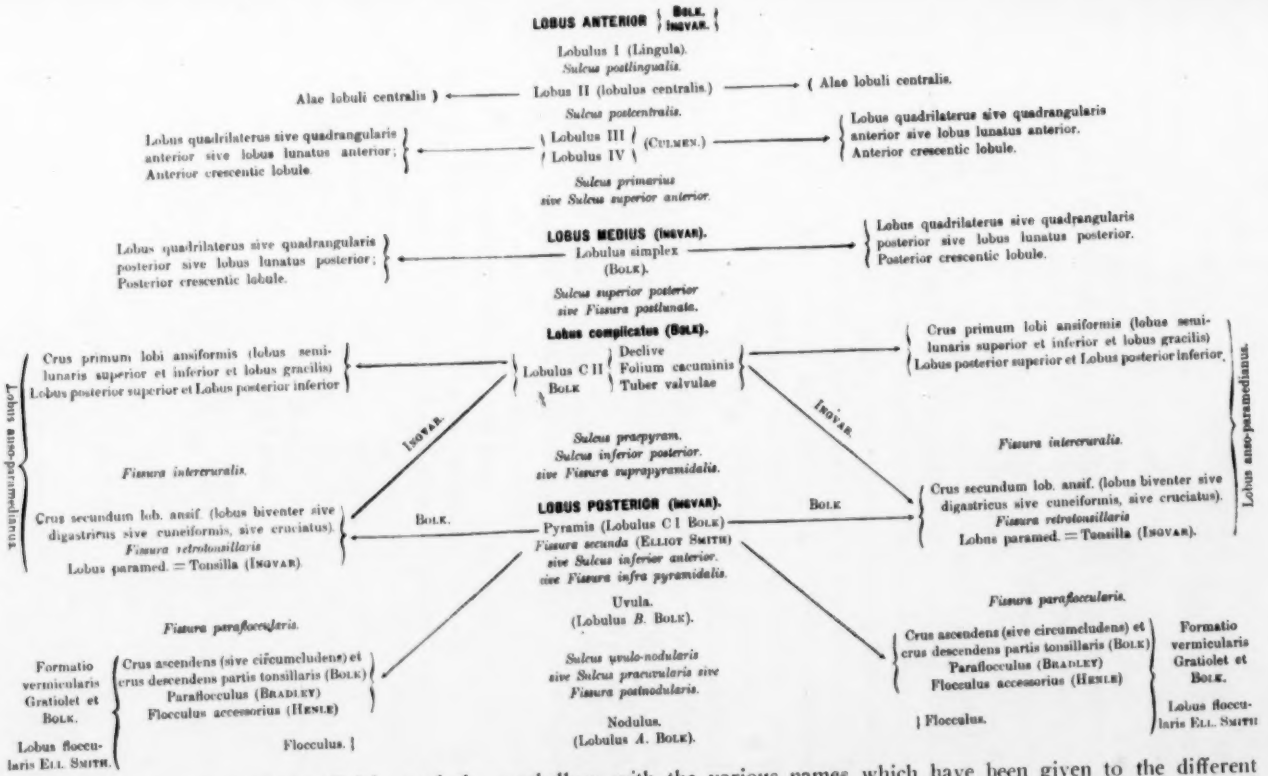


Fig. 23.—A survey of the divisions of the cerebellum with the various names which have been given to the different parts. From Kappers and Fortuyn: Vergleichende Anatomie des Nervensystems.

the meaningless terms which make the study of this part of the brain almost an impossibility. An attempt should be made to return to a simpler and more intelligible set of descriptive terms.

The present extremely unsatisfactory condition of cerebellar nomenclature can readily be understood by even a superficial survey of the collation of terms in current use made by Kappers and Fortuyn in their "Vergleichende Anatomie des Nervensystems." The impossibility of remembering such meaningless terms has led me in recent years to ignore almost completely the names of the parts of the cerebellum in the course given to the students of the College of Physicians and Surgeons at Columbia University on the morphology of the nervous system.

It would perhaps be advantageous at the outset to indicate the terms in general use in connection with the description of the anatomy of the cerebellum which should not be discarded. This organ obviously can be divided into a mesial and two lateral portions. The mesial subdivision at present is called the vermis from its resemblance to a worm, and this term can perhaps be retained. The lateral portions called hemispheres can still be so nominated. The term hilus is also of value. The purely descriptive terms applied to the surface of the cerebellum are of value not only from the gross anatomic but also from the surgical points of view, and the appellations, occipital, tentorial and petrosoventricular surfaces, may well be continued.

There can be but little doubt that no anatomist or neurologist can retain the series of names ascribed to lobuli and fissures for any length of time, except as a sheer feat of memory. There are as yet no conclusively proved physiologic data that can lend definite significance to these morphologic units. Until much more physiologic data are adduced, by which some sort of functional localization is possible in this part of the brain, it would seem wiser to try to establish a cerebellar nomenclature that will have some usefulness to the various classes of investigators who are approaching the study of the cerebellum from morphologic, embryologic and experimental points of view in order that a uniform code may be used by all.

Langelaan, in 1919, recognized this problem and endeavored to solve it by selecting the most reasonable of the terms in general use:

Fissura prelingualis
1. Lobus vinculolingualis
Fissura precentralis (f. centrolingualis)
2. Lobus centro-alaris
Fissura prelunata (f. culminocentralis)
3. Lobus culminolunatus
Fissura superior anterior (f. declivoculminalis)
4. Lobus declivolunatus
Fissura superior posterior (f. foliodeclivalis)

5. Lobus foliosemilunaris
   Fissura horizontalis (f. tuberofoliaris)
6. Lobus tuberosemilunaris
   Fissura inferior posterior (f. pyramidotuberalis)
7. Lobus pyramidobiventricus
   Fissura inferior anterior (f. uvula pyramidalis)
8. Lobus uvulatonsillaris
   Fissura preuvularis (f. nodulo-uvularis)
9. Lobus nodulofloccularis
   Fissura prenodularis (f. nodiolonodularis)
10. Lobus nodulovelaris

As shown, he manufactured a number of compound terms which indicated the vermal and hemispheral constitution of each lobulus and suggested that the fissures be named in accordance with the lobuli which bordered on each fissure. Although it simplified to a considerable extent the nomenclature of the cerebellum, this attempt still leaves the anatomist with a considerable number of terms which must be learned and depends on the accurate retention of the nominal sequence of the cerebellar subdivisions.

Bolk's classification, with certain modifications, presents the most reasonable and applicable group of terms that have been met with. In certain respects, it may perhaps be improved on.

Bolk advocated a fundamental difference between the cephalic and caudal lobes, in stating that the process of growth from centers is dissimilar in the production of these two lobes. This would not seem to be substantiated by observations that have been made by others and to which reference has been made in a preceding paper. Investigation from anatomic, embryologic and clinical points of view seems to support the conception that a similar process is at work in the production of both of these lobes.

Two features of Bolk's division of the caudal lobe will bear further discussion. In his description, Bolk divided the caudal lobe into a cephalic portion, the lobulus simplex, and a caudal subdivision, the lobulus complicatus. The necessity for the retention of the lobulus simplex does not seem to be evident. This lobulus is composed of the most cephalic portion of lobulus C 2. It is not constantly present and in fact seems to be more persistently absent in the cerebella that have already been reported. It is extremely variable, the only class of mammals in which it is at all recognizable being the ungulates. This portion of the caudal lobe, therefore, seems to be variable, and in the primates and man there is no clearly homologous lobulus simplex. It would seem wise, therefore, to discard this differentiation.

The numerous divisions of the formatio vermicularis already mentioned may have value from strictly comparative morphologic standpoints, but they have but little applicability to human anatomy, and therefore for this purpose they may be ignored.

From many points of view, a classification modified along these lines would seem to meet the necessary requirements. Bolk's classification pays little heed to the fissures separating the constituent parts of his cerebellar schema. Other investigators have recognized the seeming necessity to name these lines of separation and have applied terms more or less difficult to remember. No important necessity seems to require the naming of these fissures and, with the exception of a few, these terms may be dropped. The separation of the cephalic and caudal lobes is of course important, and the term fissura primaria answers all requirements. There does not appear to be any definite reason why the lines of separation between lobuli 1 and 2 and lobuli 2 and 4 should receive any special designation. In the caudal lobe, the early differentiation of the flocculus from the paraflocculus is important, and this fissure can be termed the paraflocculo-floccular fissure, while the differentiation between lobulus C and lobulus B can be called the fissura secunda in both its vermal and its hemispheral portions. The great horizontal fissure would better be called the sulcus intercruralis. The other fissures gain nothing but confusion and endless complexity by receiving names that mean nothing except their anatomic positions and have no physiologic significance. The lines of differentiation between the vermal and hemispheral portions of the lobules, now called the vallecula dextra and the vallecula sinistra, can be nominated the sulcus paramedianus dexter and the sulcus paramedianus sinister. The discarding of meaningless anatomic terms and the adoption of a reasonable group of names that can be used by all investigators without too great a tax on the memory will result in a much clearer comprehension of cerebellar morphology.

The lobules of the cephalic lobe of the cerebellum in the mammalian order are designated by Bolk by number, from 1 to 4 in a cephalocaudal direction. The constant lobules are 1, 2 and 4, number 3 appearing only inconstantly but sufficiently often to require recognition. Owing to the belief which he held that the hemispheral portions were only outgrowths from the vermal focus, Bolk gave no separate designations to these portions of the cerebellum. This would seem to be an error, and it is suggested that the parts be differentiated by the use of the localizing terms, vermalis and lateralis, for example, lobulus 2 vermalis or lobulus 4 B lateralis. This method of designating the lobules is simple, open to no misunderstanding and easily remembered.

Lobulus 1 vermalis corresponds to the human lingula. Its lateral extensions are more or less rudimentary, and when they exist may be

termed lobulus 1 lateralis, corresponding to the frenulum lingulae. Lobulus 2 vermalis is the lobulus centralis, and it presents a lateral portion which may be called lobulus 2 lateralis, the ala lobuli centralis of human morphology. Lobulus 4 vermalis is the human culmen and would better be recognized by the former term, while its lateral extension, corresponding to the anterior lunate lobule of human anatomy, may be called lobulus 4 lateralis.

In considering the constituents of the caudal lobe, Bolk recognized the vermal and hemispheral contributions as being of separate origins, and he devised a fairly simple but consistent terminology for these parts. In view of the evident homology which seems to exist between the various parts of the cerebellum throughout the mammalian order and considering the great advantages to be derived by discarding the ponderous nomenclature of human morphology, it would appear to be advantageous to advocate the use of a modification of Bolk's nomenclature for the comparative cerebella in the description of the human organ.

The vermal subdivisions, as seen on median section, are arranged as three main lobules which are named in a cephalocaudal direction as lobulus C, B and A. In certain of the cerebella examined, modifications have been noted in lobuli C and B, and at times these have been subdivided into C 2 and C 1, B 2 and B 1. In the arbor vitae of the human cerebellum, these same subdivisions are clearly recognizable, and their designations as C, B and A would appear to be adequate. The hemispheral portion, however, is not so evidently comparable to Bolk's schema unless the orderly progression of the evolutional process has been carefully followed and the gradual transitions appreciated. With this course of events clearly in mind, the grossly altered human constituents fall into their natural places, and one is able to designate the various parts with the same names that have been used in comparative terminology.

The clivus and the folium cacuminis represent that part of lobulus C 2 which lies cephalad to the great horizontal fissure, the homolog of the sulcus intercruralis, and would be better called lobulus C 2 vermalis, presulcal. The lamella of the hemispheres which are connected with the clivus and the folium cacuminis form the lobulus lunatus posterior and the lobulus posterosuperior of human morphology. Lying cephalad to the sulcus intercruralis, they represent crus 1 and may better be so nominated.

The remaining portion of lobulus C 2 in the vermis lies caudal to the sulcus intercruralis and is named the tuber valvulae. This part of the vermis may be called lobulus C 2 vermalis, postsulcal. Its lateral extensions form the lobulus postero-inferior, the lobulus gracilis posterior and the lobulus gracilis anterior. These hemispheral components,

lying caudal to the sulcus intercruralis and connected with this vermal portion of lobulus C 2, therefore represent crus 2 and should be so called.

Lobulus C 1 represents the pyramis, while the lateral extension, named the lobulus biventer, represents the lobulus paramedianus. The fissura secunda intervenes here, separating lobulus B from lobulus C.

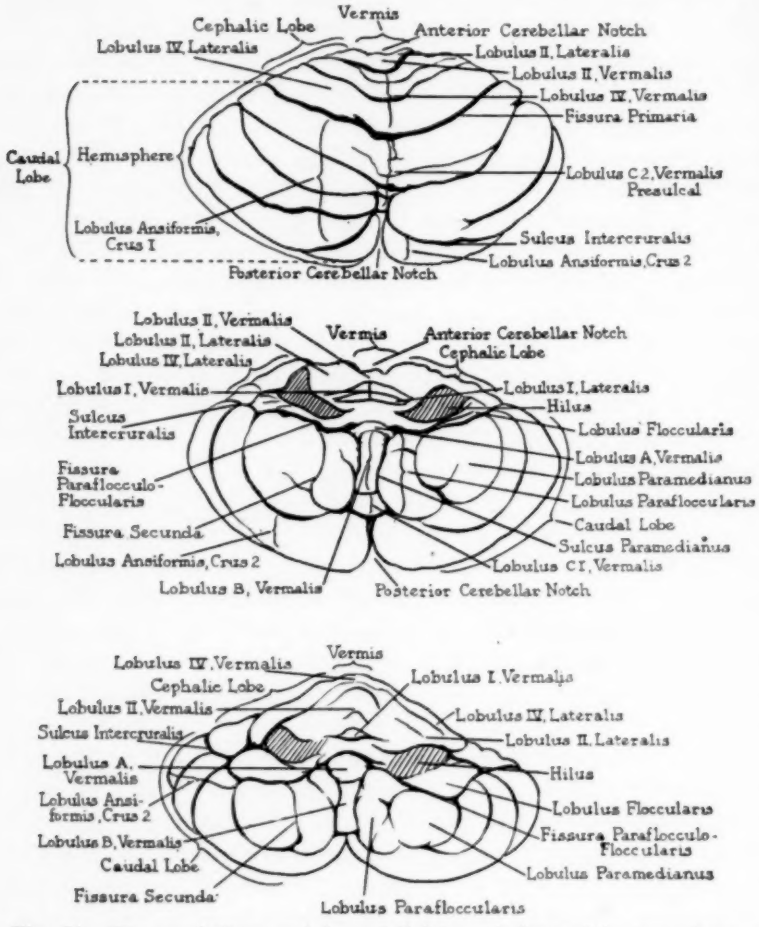


Fig. 24.—The cerebellum and its subdivisions designated in accordance with the modified nomenclature of Bolk. The upper figure represents the tentorial surface, the middle figure the occipital surface and the lower figure the petrosoventricular surface of the cerebellum.

Lobulus B represents the uvula, and the parts connected with it in the hemisphere homologize with the human tonsil, the lobulus parafloccularis of Eliot Smith and Bradley and the formatio vermicularis of Bolk. In this instance the term lobulus parafloccularis seems to be better.

Lobulus A, corresponding to the nodulus, is connected with the lobulus floccularis or flocculus and should bear the former name.

The synonyms for the hemispheral portions of the cerebellum are so extensive and so confused that much would be gained by dropping all of them and substituting terms that have a definite comparative morphologic significance. Of those advanced by various anatomists, it would be difficult to choose any one, and it would seem advisable to discard the entire mass of names and use those which have some evolutional significance.

The most desirable solution would seem to be the selection of terms which not only the human anatomist, but also the comparative morphologist, the embryologist and the physiologist would combine on as being the simplest and most applicable to all of the problems of cerebellar study and investigation. With this end in view, the following schematization of the constituents of the cerebellum and a simplified group of terms is suggested.

CEPHALIC LOBE

Vermis	Hemisphere
Lobulus I vermalis (Lingula)	Lobulus I lateralis (Frenulum Lingulae)
Lobulus II vermalis (Lobulus Centralis)	Lobulus II lateralis (Ala Lobuli Centralis)
Lobulus IV vermalis (Culmen)	Lobulus IV lateralis (Lobulus Lunatus Anterior)

Fissura Primaria

CAUDAL LOBE

Lobulus C 2 vermalis, presulcal (Clivus) (Folium Cacuminis)	Lobulus Ansiformis, Crus 1 (Lobulus Lunatus Posterior) (Lobulus Postero-Superior)
Sulcus Intercruralis (*Great Horizontal Fissure*)	
Lobulus C 2 vermalis, postsulcal (Tuber Valvulae)	Lobulus Ansiformis, Crus 2 (Lobulus Postero-Inferior) (Lobulus Gracilis Posterior) (Lobulus Gracilis Anterior)
Lobulus C 1 vermalis (Pyramis)	Lobulus Paramedianus (Lobulus Biventer)
Fissura Secunda	
Lobulus B vermalis (Uvula)	Lobulus Paraflocculus (Tonsil)
Fissura Paraflocculo-Flocculus	
Lobulus A vermalis (Nodulus)	Lobulus Flocculus (Flocculus)

In the experience of many teachers, it has been found inadvisable to insist on the recognition of the various parts of the cerebellum as they are named in human anatomy, since it is impossible to retain the names for any length of time. If definite functions could be ascribed to the units it would be another matter, and results might warrant this exercise of the memory. The investigation of the cerebellum is still being actively pursued by research workers the world over, and this failure of uniformity of terms seriously handicaps the value of their work. The present suggestions provide a common ground for description and would clear up much of the ambiguity at present found in following cerebellar investigation.

Whether further reflection will sustain the present belief that the retention of only the comparative terms will be satisfactory is uncertain, but a simplification of the terms in use is urgently needed.

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THE RED NUCLEUS AND ADJACENT CELL GROUPS

A TOPOGRAPHIC STUDY IN THE CAT AND IN THE RABBIT *

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Experimental work on the brain should be based on an accurate knowledge of form and structure. This should go beyond a mere familiarity with surface form and typical sections and should include a tridimensional conception of the size, shape, form and relations of the nuclei and fiber tracts. Physiologic studies which make use of transection of the brain stem require the recognition of the internal structures involved in the section in order that possible functions of each structure can be evaluated. In making a transection, external structures must be used as guides; hence we have endeavored to make a reconstruction of the region of the red nucleus which would indicate its relationships to external landmarks. The cat and rabbit have been chosen because they are the most popular animals for the study of phenomena involved in decerebration experiments.

Monakow [1] recognized in the red nucleus of the rabbit a large cell division (ventrally placed), a nucleus dorsalis reticularis, a dorsolateral recticular portion (N. gelatinosus), a nucleus minimus and a lateral horn. This arbitrary division was seen in a section through the middle third. In the anterior third only the first three divisions were seen. In the cat, in a section through the middle third a magnocellular division was seen, and the lateral horn was said to be fused with the nucleus gelatinosus. Foix and Nicolesco [2] found it difficult to systematize these divisions in the mouse, rabbit, guinea-pig, sheep and dog.

Hatschek's [3] studies led to the conclusion that the red nucleus in mammals consisted of a large cell caudal and small cell rostral part. The large cells were most prominent in lower mammals, while the small cells predominated in man.

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1. Monakow, C.: Der rote Kern, die Haube und die Regio subthalamica bei einigen Säugetieren und beim Menschen, Arb. a. d. hirnanat. Inst. in Zurich, pt. III, Munich, J. F. Bergmann, 1909, p. 49.

2. Foix, C., and Nicolesco, J.: Anatomie cérébrale, les noyaux gris centraux et la région mésencéphalo-sous-optique, Paris, Masson & Cie, 1925.

3. Hatschek, R.: Zur vergleichenden Anatomie des Nucleus ruber tegmenti, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **15**:89, 1907.

According to the atlases of Winkler and Potter,[4] there are no well defined large and small cell components of the red nucleus of the cat and rabbit. The cells of different sizes are mixed, but the large cells predominate in the caudal pole of the nucleus. The nucleus appears to extend further rostrad in the cat than in the rabbit. The tip of the mammillary body appears in plate XVI (rabbit) and plate XV (cat) of the atlas. At this level the rostral tip of the red nucleus is no longer present in the rabbit but appears in the cat in plate XV and even in plate XIV (proceeding rostrad).

The present study was undertaken to provide an accurate chart of the location (with particular reference to its rostral limits) of the red nucleus in both cat and rabbit. It seemed evident from the charts of Winkler and Potter and from the diagrams of Magnus [5] that the red nucleus extended farther rostrad in the cat, with reference to external structures, than in the rabbit. A difference in structure of the two brains might serve to explain the difference in tonus shown by the two animals after transection of the brain stem through similar external structures.

Rademaker [6] transected the brain stem of both cats and rabbits through varying levels and found that cats exhibited rigidity (2 of 4 animals) when the section passed through the rostral portion of the superior colliculi dorsally to just rostral to the exit of the oculomotor nerve ventrally. The other two cats appeared to have suffered from operative shock. All rabbits showed no rigidity after a similar section.

Hinsey, Ranson and McNattin [7] found that cats were able to walk and climb after a section of the brain stem which passed from the anterior border of the superior colliculi through the optic chiasma. If the section passed from the same dorsal level to the caudal border of the mammillary bodies, the animals exhibited rigidity and had lost the ability to maintain an upright posture.

A study which involved the region of the red nucleus was made by Ranson, Hinsey and Taylor [8] on the crossed extensor reflex in cats. Quick relaxations of the deafferented gastrocnemius were obtained when

4. Winkler, C., and Potter, A.: An Anatomical Guide to Experimental Researches on the Rabbit's Brain, Amsterdam, W. Versluys, 1911; An Anatomical Guide to Experimental Researches on the Cat's Brain, Amsterdam, 1914.

5. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924, p. 599.

6. Rademaker, G. G. J.: Die Bedeutung der roten Kerne und des übrigen Mittelhirns für Muskeltonus, Körperstellung und Labyrinthinthreflexe, Berlin, Julius Springer, 1926.

7. Hinsey, J. C.; Ranson, S. W., and McNattin, R. F.: The Rôle of the Hypothalamus and Mesencephalon in Locomotion, to be published.

8. Ranson, S. W.; Hinsey, J. C., and Taylor, L. A.: The Crossed Extensor Reflex in Deafferented Muscle, Am. J. Physiol. **88**:52 ,1929.

the brain stem was sectioned at the upper border of the mesencephalon, but a prolonged contraction was the response obtained when the transection was made near the upper border of the pons. This study indicated that a part of the mechanism which regulates tonus was contained in the mesencephalon and that its function was chiefly inhibitory. This inhibitory mechanism was still in good functional condition after the diffuse part of the red nucleus which lies rostral to the third nerve had been removed.

In the present study we have been interested chiefly in the extent and distribution of the large cells of the red nucleus and the other cell aggregations that lie immediately rostral to it. The reconstructions shown in figures 1 and 2 represent the locations of nuclei as they would appear in profile from a medial saggital section if the brain stem were considered transparent.

The material studied consisted of one set of serial cross-sections of the midbrain of the cat and one of the rabbit. The sections were made from formaldehyde fixed material embedded in celloidin and cut 30 microns thick. Every third section of each series was stained for myelin sheaths (Weil's [9] method) and the other two for cells (one neutral red and one cresyl violet).

In order to supply the third dimension of the reconstruction and provide a suitable outline for orientation of the cross-sections, a midsagittal section of another brain stem of each species was prepared from material which had been fixed and dehydrated in the same manner as the material from which the cross-sections were prepared.

The reconstructions were made by the following procedures: A midsagittal section was photographed on a lantern slide and projected. The size of the projected section was adjusted until each millimeter of its length was equivalent to the thickness of one 30 micron cross-section of the series to be studied. This scaling was accomplished by selecting two characteristic landmarks (anterior border of the posterior commissure and posterior border of the posterior colliculus), finding the number of serial cross-sections between the two and adjusting the image of the midsagittal section until the distance in millimeters between these points was equal to the number of cross-sections included. The plane at which the cross-sections were cut was determined by dorsal and ventral landmarks and lines (for every third cross-section) drawn across the traced outline of the midsagittal section. The lines were numbered according to the serial cross-sections and the location of a given structure was finally made by measuring its position with an ocular micrometer. Distortions in measurements by the latter were found to be least

9. Weil, A.: A Rapid Method for Staining Myelin Sheaths, Arch. Neurol. & Psychiat. **20**:392 (Aug.) 1928.

when the outlines of the third ventricle and ventral surface of the cerebral aqueduct were used for orientation lines rather than the outlines of the external surfaces.

The outlines of the nucleus interstitialis, the zona incerta and the nucleus subthalamicus might be placed with some variation in location and extent by different investigators using the same material for study, because these cell aggregations blend with the reticular formation of the region and other nuclei.

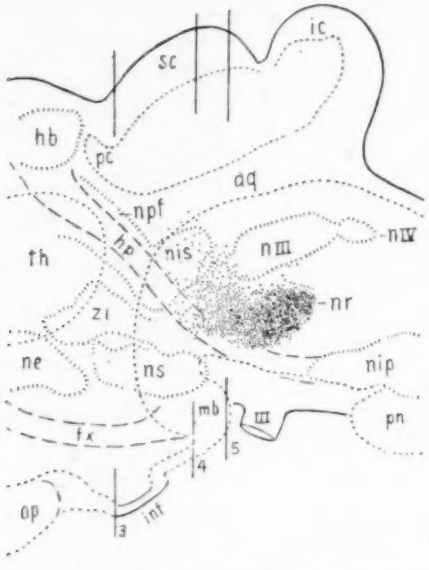

Fig. 1.—Reconstruction of a lateral view (as seen from a sagittal section) of the mesencephalon of a cat. The abbreviations in this and the following figures indicate the following:

aq cerebral aqueduct
cp cerebral peduncle
cgs central gray stratum
fl fasciculus lenticularis
fx fornix
hb habenula
hp habenulopeduncular tract
ic inferior colliculus
inf infundibulum
mb mammillary body
mg medial geniculate body
ml medial lemniscus
mt mammillothalamic tract
nD nucleus of Darkschewitsch
ne entopeduncular nucleus (globus pallidus)
nip interpeduncular nucleus
nis interstitial nucleus (of Cajal)
npf parafascicular nucleus
n III oculomotor nucleus
n IV trochlear nucleus
nr red nucleus
ns subthalamic nucleus
op optic tract
pc posterior commissure
pn pons
sc superior colliculus
sn substantia nigra
stg substantia tegmentalis
th thalamus
v III third ventricle
zi zona incerta
III oculomotor nerve

RED NUCLEUS

The red nucleus has been indicated by dots, each of which represents a cell of about 40 microns or more in diameter (figs. 1 and 2). The object of this type of representation was to show the distribution of the large cells of the nucleus rather than the exact number. It can be seen that the well known caudal pole has the large cells densely packed. There are relatively few small cells in this part of the nucleus. The rostral portion of the nucleus is diffuse, and the large cells are

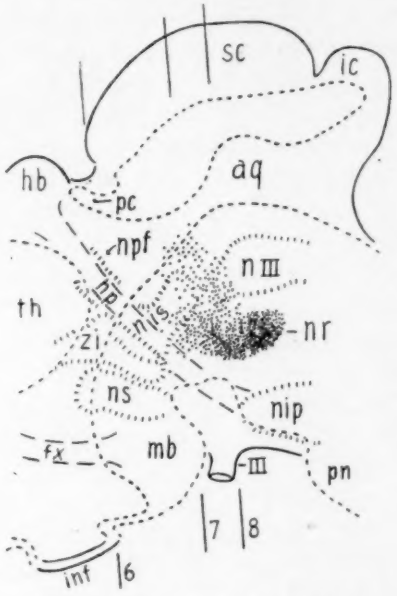

Fig. 2.—The same in a rabbit.

found as far dorsal as the level of the aqueduct. The small cells appear no more numerous in this region than in the reticular formation. Near the middle portion of the nucleus, however, the smaller cells appear to be somewhat more compact than in the reticular formation outside. There is no striking difference in forms of the nuclei in the two species studied. We have been unable to identify any definite rostral small-celled portion of the red nucleus in the cat or rabbit, although such a structure is frequently mentioned in the literature. Likewise, we have been unable to see any advantage gained by subdivisions of the nucleus other than a compact and a diffuse portion. The fibers from the oculomotor nucleus and arcuate fibers from the tectum in passing through the red nucleus cause adventitious divisions which vary from section to section but have no anatomic continuity. The nucleus minimus, a compact group of several dozen tiny cells, was seen near the lateral margin

of the middle of the red nucleus in the cat, but could not be identified with certainty in the rabbit. An appreciable condensation of small cells was seen in the reticular formation lateral to the rostral third of the red nucleus. This nucleus (if we may recognize it as such) is figured by Winkler and Potter for the rabbit (N. lateralis substantio reticularis) but is not shown for the cat unless it is their nucleus ventralis *a* of the thalamus (plate XV). This cell aggregation is one of the structures that might conceivably be regarded as a small cell component of the red nucleus in the cat and rabbit. Another group of small and medium-sized cells lies medial and somewhat dorsal to the rostral border of the diffuse portion of the red nucleus, occupying a location which appears to be the same as the nucleus of Darkschewitsch figured for the rabbit by Winkler and Potter and the nucleus interstitialis for the cat by Papez.[10] These two nuclei are illustrated in figures 3 *B* and 4 *B*. Since there seems to be some uncertainty as to the location of the nucleus of Darkschewitsch and interstitial nucleus, we have figured them as shown originally by Cajal.[11] The cell aggregations shown in figures 3 *B* and 4 *B* appear to be homologous in the two species.

NUCLEUS INTERSTITIALIS

This concentration of cells lies immediately adjacent to the central gray stratum. In cross-section it occupies a position with reference to the central gray stratum similar to that of the oculomotor nucleus, except that it is more lateral and dorsal. Its caudal limit is found near the medial portion of the rostral pole of the red nucleus, and it extends rostrad to the habenulopeduncular tract where it is pierced by it. In this region the cellular pattern becomes somewhat different in the cat from that in the rabbit. The interstitial nucleus appears to fuse with the nucleus of the habennulopeduncular tract in the former but not in the latter. In both species its rostral position comes into close relationship with the caudal part of the thalamus.

NUCLEUS PARAFASCICULARIS

This is the nucleus tractus Meynert shown by Winkler and Potter in the cat, but it is not figured by them in the rabbit. It seems to us that its peculiar annular structure around the tract suggests merely a displacement of cell masses in the region the tract pierces rather than its having synaptic connections with the habenulopeduncular tract itself.

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10. Papez, J. W.: Comparative Neurology, New York, Thomas Y. Crowell Company, 1929.

11. Ramón y Cajal, S. R.: Histologie du système nerveux de l'homme et des vertébrés, Paris, A. Maloine, 1911, vol. 2, p. 492.

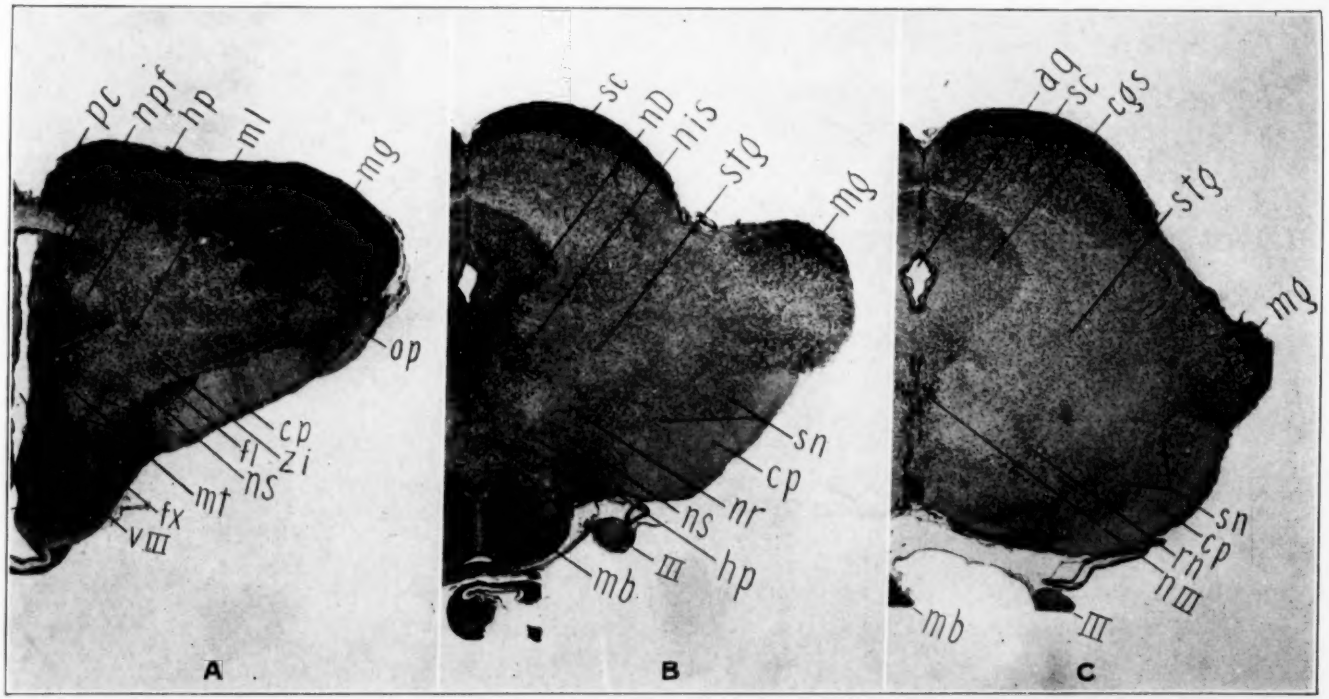

Fig. 3.—Reproductions of photomicrographs of cross-sections (cresyl violet stain) of the mesencephalon of a cat. The levels of section shown by the arabic numerals 3, 4 and 5 in figure 1 correspond to *A*, *B* and *C* in this figure; the magnifications are 5¼, 6½ and 7, respectively.

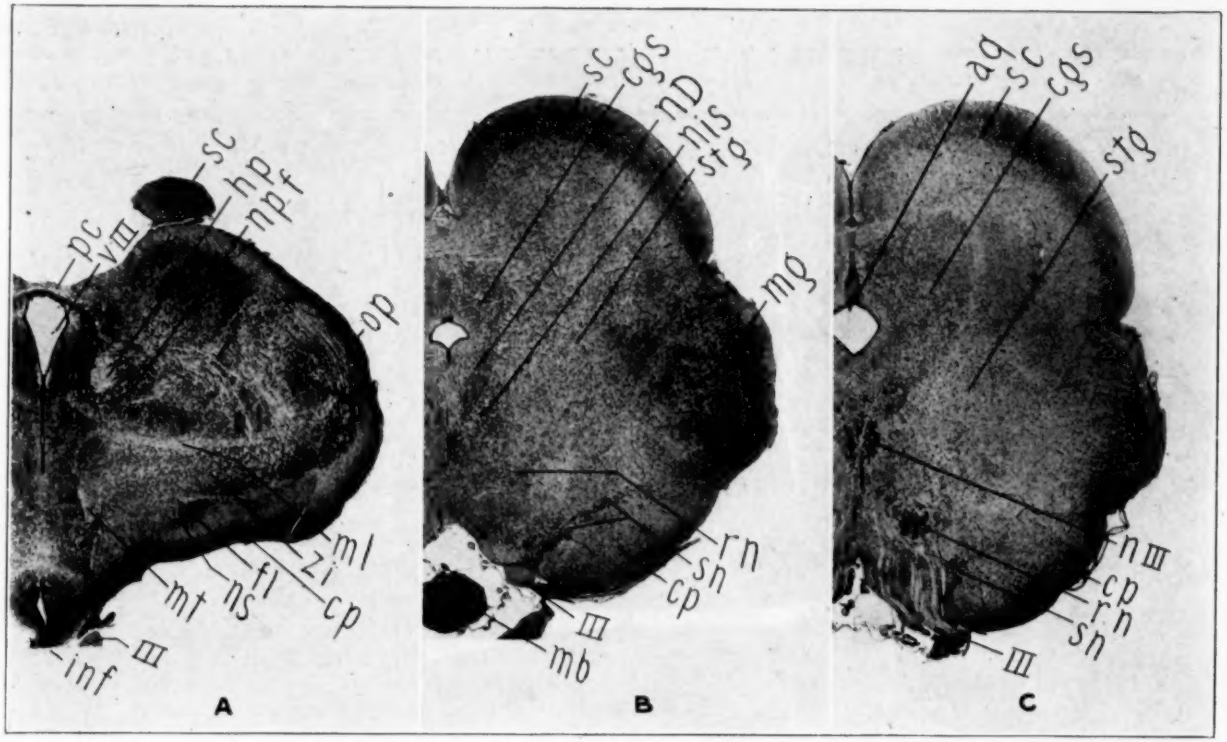

Fig. 4.—The same in a rabbit. The levels of section shown by 6, 7 and 8 in figure 2 correspond to *A*, *B* and *C* in this figure; the magnifications are 7½, 8 and 9, respectively.

Our preparations show its presence in the rabbit, but its chief representation is in the region of the rostral pole of the interstitial nucleus and the caudal pole of Winkler and Potter's *centre médian* of the thalamus. The same relationships are present in the cat, except that the proximity of the two nuclei makes it appear that the cell mass around the habenulopeduncular tract is more continuous.

SUBTHALAMIC NUCLEI

Zona Incerta.—The region has been plotted in figures 1 and 2 to include the Forel fields H_1 and H_2 as well as that portion which lies between them. This interpretation is in agreement with Dejerine,[12] Foix and Nicolesco,[2] and Gurdjian.[13] It likewise corresponds to the reticular subthalamic nucleus of Papez, and includes the nucleus peripeduncularis lateralis of Jacobsohn (figured by Malone[14] and by Papez[10]) and the corpus subthalamicum of Winkler and Potter and the zona incerta shown in Marburg's[15] atlas. According to Crosby,[16] it is possible to identify a caudal division (zona incerta caudalis) which is separated from the zona incerta proper by fiber bundles which include fascicles of the dorsal supra-optic system. The latter area extends medially to the field H_1 of Forel and lies along the dorsolateral border of the peduncle. The guide line of the label in figure 3 *A* crosses the lateral tip of the subthalamic nucleus, the fasciculus lenticularis, then the zona incerta proper and finally touches the under limit of the zona incerta caudalis. In this region, the zona incerta caudalis fuses medially with the fields of Forel.

Nucleus Subthalamicus (of Luys).—The cell mass which lies medial and dorsal to the cerebral peduncle at the caudal margin of the mammillary body may be taken as the caudal pole of this nucleus (figs. 3 *A* and 4 *A*). In both species it appears to be a continuation of the substantia nigra and in fact shows no division from this cell column in the rabbit. In the cat there is some thinning of the cells of the substantia nigra in the region of the caudal pole of the mammillary body and then an increase in density of the column to form the subthalamic nucleus as it proceeds rostrad. The cells of the nucleus do not appear

12. Dejerine, J.: Anatomie des centres nerveux, Paris, J. Rueff, 1901, vol. 2, p. 407.

13. Gurdjian, E. S.: The Diencephalon of the Albino Rat, J. Comp. Neurol. **5**:43, 1927.

14. Malone, E.: Ueber die Kerne des menschlichen Diencephalon, Verlag der Königl. Akad. der Wissensch., Berlin, 1910.

15. Marburg, O.: Mikroskopisch-topographischer Atlas des menschlichen Zentralnervensystems, Vienna, Franz Deuticke, 1904.

16. Crosby, Elizabeth C.: Personal communication, 1929.

to differ essentially from other small stellate and oblong cells of the reticular formation. It continues rostrad to a plane of cross-section which passes near the middle of the infundibulum and is terminated in part by fusion with the zona incerta and in part by the dorsal inclination of the peduncle. This nucleus is figured as the nucleus proprius pedunculi cerebri by Winkler and Potter, but there is good agreement among other authors on the names, subthalamic nucleus of Luys and corpus luysi.

OTHER NUCLEI

The intrapeduncular and peripeduncular nuclei (figured for the cat by Papez) have been included in the zona incerta. The peripeduncular nucleus shown by Malone [14] (fig. 7, plate IV) appears to correspond to the zona incerta figured by Marburg [15] (cross-section 21, plate XIV).

The nucleus of Darkschewitsch consists of the group of small cells which occupies the ventrolateral portion of the central gray stratum in the region of the interstitial nucleus.

The entopeduncular nucleus shown in figure 1 (cat) could be identified in the rabbit at a somewhat higher level than is included in figure 2. This cell group may be homologous to the globus pallidus in man and is figured by Winkler and Potter as a part of the globus pallidus for both cat and rabbit. We have traced the structure rostrad in the cat and found that it came into immediate relationship with the larger structure usually regarded as the globus pallidus. It seems probable that the entopeduncular nucleus is, in the cat, a caudal extension of the globus pallidus, because both possess the same type of elongated large cells. The structure is called the olfactory striatum by Papez.

SUMMARY

1. The nuclei of the tegmentum and subthalamus of the cat and the rabbit occupy approximately the same levels; hence any difference in behavior noted between the two species after transection at the same level is not explained by anatomic differences.

2. The red nucleus is similar in both species and may be conveniently divided into a compact caudal and a diffuse rostral part.

3. The small cells within the magnocellular field are most numerous near its center, that is, the region adjacent to the rostral fibers of the root of the third nerve.

4. There was no definite parvocellular division of the red nucleus in the two species studied.

THE NUCLEI OF THE REGION OF THE TUBER CINEREUM

DEGENERATIVE CHANGES IN CASES OF EPILEPSY, WITH A DISCUSSION OF THEIR SIGNIFICANCE*

LAWRENCE O. MORGAN, PH.D.

CINCINNATI

Some time ago I began an experimental investigation of the nuclei of the subthalamic and hypothalamic regions of the brain of the dog. Lesions were made in these regions by the injection of a weak solution of mercuric chloride or silver nitrate. Of the series of dogs originally used, the lesion in five cases lay within an area in the wall of the third ventricle extending from the optic chiasm to the mammillary bodies and reaching dorsally to the thalamus. These animals, normal at first, developed a series of convulsions after a few hours. The convulsions usually became more severe and more frequent, resulting in the death of the animal several hours after the onset of symptoms. They were characterized by muscular spasms, salivation, dilatation of the pupils, vasoconstriction, increase in heart rate, a rise in temperature and unconsciousness. A brief summary of this work is needed here to introduce the main topic of this article.

In collaboration with Clarence A. Johnson,[1] a series of experiments is being conducted with a view to determining the symptomatology and changes in blood chemistry following lesions in the tuberomammillary region of the brain. An attempt is also being made to determine, as far as possible, the function and fiber connections of the nuclei located in this region (the nucleus tuberomammillaris, tuberis lateralis and substantia grisea of the third ventricle). A lesion has been successfully placed in seventeen animals. It soon became apparent that the convulsions which occurred in these experimental animals were almost identical with those which characterize idiopathic epilepsy.

Apparently normal in other respects, these animals had periodic convulsions which began a few hours after the operation. The animal would become confused, the pupils dilate, the skin become blanched, and excessive salivation begin. Following these symptoms almost instantaneously, the animal would become rigid and plunge forward or fall on its side unconscious. The rigidity would soon give place to clonic spasms. The convulsions were further characterized by increased heart rate, rise in temperature, erection of the penis, frequently by micturation and

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1. Morgan, L. O., and Johnson, C. A.: Symptoms Resembling Epilepsy Following Experimental Lesions in the Brain of the Dog, Proc. Soc. Exper. Biol. & Med. **25**:442, 1928.

occasionally by defecation. The fit itself usually lasted from one and a half to three minutes, after which the animal was confused and disoriented for several minutes. Sometimes light convulsions occurred in which the animal did not fall or lose consciousness, and the muscular spasms affected particularly the fore part of the body. In some cases the convulsions would begin rather lightly a few hours after the operation and would occur at intervals of from forty to sixty minutes. These fits would then become more frequent and more severe until the animal passed into a continuous state of coma with convulsions occurring every few seconds. At this later stage, resembling status epilepticus in the human, the heart rate was increased to from 200 to 250, the temperature rose to from 105 to 110 F., and in a few cases in which the abdomen was open the intestines and stomach were observed to be flaccid and the bladder moderately contracted. Some animals had periodic fits lasting from one to three days, after which the animal recovered completely. In two animals a cannula was placed in the carotid artery and the blood pressure and heart rate were recorded on a smoked drum along with a writing of the muscular spasms. This experiment showed that a rise in blood pressure and increase in heart rate momentarily preceded the muscular spasm. This characteristic group of symptoms occurred only in the cases in which the lesion involved an area containing the substantia grisea of the third ventricle, the nucleus tuberis lateralis and nucleus tuberomammillaris.

The blood changes of eight animals which developed the typical symptoms described, and which on subsequent histologic examination were shown to have definite lesions in the region of the tuber cinereum, were carefully studied. Briefly, the following observations were made: 1. Neither the calcium or potassium content of the serum nor the potassium: calcium ratio was appreciably altered. 2. Nonprotein nitrogen seemed to increase with the severity of the convulsions, but the results were not entirely constant. 3. Urea nitrogen followed the trend of nonprotein nitrogen but was even less constant. 4. The carbon dioxide combining power of the plasma decreased as the frequency and severity of the fits increased. 5. Blood sugar changes were by far the most definite observations. Invariably the sugar content rose steadily to about twice the normal value; then, as the frequency and severity of the spasms increased, the value decreased until the animal died in a state of coma. Sugar values a few minutes before death were often only one half of the normal value. The absence of glycogen in the liver (only two animals were examined) probably indicates the complete mobilization of this carbohydrate into the blood stream. The animals which did not develop the typical symptoms and which showed no lesions in the said nuclei were used as controls and were considered normal.

In some recent work I am attempting to determine what relation, if any, the internal secreting glands have to the symptoms which follow experimental lesions in the infundibular region of the brain. Only five successful experiments have been completed to date. Lesions were placed in the tuber cinereum of the brain in dogs. After the convulsions had progressed until they were occurring at frequent and regular intervals the blood supply to the thyroid, parathyroid and suprarenal glands was clamped off and the effect on the symptoms noted. It was found that clamping off the blood supply to the thyroid and parathyroid caused almost instantaneous cessation of the muscular spasms and a lowering of body temperature, but did not alter the remaining symptoms. On the other hand, when the blood supply to the suprarenals was clamped off, the intestines and stomach (previously flaccid) constricted and began peristalsis; the pupils constricted, and the heart rate was reduced to approximately normal. In either case clamping off the

blood supply to the gland on one side showed a marked effect on the symptoms but did not cause a return to normal. In these experiments the animals were too severely injured to recover completely, but in two cases there was a partial return of consciousness following the clamping off of the suprarenals. Clamping off the suprarenals caused the muscular spasms to become less severe but did not eliminate them entirely. During the course of these experiments two animals were obtained which showed the usual symptoms except that the muscular spasms were almost entirely absent. In one of these cases, clamping off the suprarenals caused a cessation of the symptoms. The case proceeded for several hours with the characteristic symptoms of hyperactivity of the suprarenal glands, following which there was a sudden relapse, the heart rate becoming subnormal, the peripheral vessels dilated, the pupils constricted, and the animal suffered a partial loss of consciousness. At this stage the animal showed, temporarily, almost complete recovery following an injection of epinephrine. This was repeated successfully a second time.

The work just described, previously published in abstract form,[2] will be reported fully in separate papers. This summary is here included in order that the experimental data may be considered in their relationship to the pathologic material described in this paper.[3]

MATERIAL AND METHODS

The results obtained in an experimental study of the tuberomammillary region of the diencephalon introduced the question whether the nuclei of this region might not be affected in human epilepsy. The present study is based on six brains from patients suffering with idiopathic epilepsy. As I believe that a study of this particular region of the brain in a large number of cases will be of more value than an extensive study of the entire brain in a few cases, I have dealt almost exclusively with changes occurring in the region of the tuber cinereum. In collaboration with Dr. H. S. Gregory, I am collecting a still larger series which will be made the subject of a later report.

A portion of the brain including the region of the third ventricle and parts of the thalamus and corpus striatum was embedded in celloidin and sectioned 50 microns in thickness. Some of the sections were stained by the iron hematoxylin and neutral red method previously described by me.[4] Other sections were stained with neutral red alone as a cell stain. The method which has proved most useful for study of the nuclei of the infundibular region is a modification of the iron hematoxylin technic. Celloidin sections were mordanted for five minutes in 4 per cent iron alum (ferric ammonium sulphate), rinsed in water and stained for

2. Morgan, L. O.: Further Observations on Mammillo-Infundibular Region of Diencephalon: Relation to Epilepsy, Dementia and the Psychoses, Proc. Soc. Exper. Biol. & Med. **25**:617, 1928. Morgan and Johnson (footnote 1).

3. Morgan, L. O.: Localized Cell Destruction and Degenerative Processes in the Brain in Odiopathic Epilepsy, Proc. Soc. Exper. Biol. & Med. **25**:444, 1928 (footnote 2).

4. Morgan, L. O.: Iron Hematoxylin as a Myelin-Sheath Stain and Neutral Red Ripened by Colon Bacillus as a Nerve Cell Stain, Anat. Record **32**:283, 1926.

thirty minutes in a 0.5 per cent solution of hematoxylin. The sections were then rinsed in a solution of sodium bicarbonate, ammonia or other alkaline reagent in order to give them an alkaline reaction. Differentiation was then carried out in a 1 per cent solution of hydrochloric acid. The best results were obtained when the sections were transferred two or three times from acid to alkali during the destaining process. Since the sections were of a faint purple in the acid solution, some experience was necessary before the differentiation could be stopped at the proper point. That point is best determined by examining the nerve cells under the microscope. The sections were then washed in the alkaline solution. In these preparations an excellent fiber stain is obtained as well as a satisfactory stain for the nerve cells. The nuclei of the glia cells are also well stained. Sections of the normal brain have been prepared in the same manner as the pathologic material and used for comparison.

The distribution of the cells in the tuber region of the brain is such that a reduction in the number of cells can be determined only by careful comparison with a section from a normal brain taken as nearly as possible at the same level. The same is true of estimating any increase in the number of glia cells. The cells of the substantia grisea are distributed fairly homogeneously throughout the area occupied by that nucleus so that the extent of the cell loss can be determined with a fair degree of accuracy. The cells of the nucleus tuberis lateralis and the nucleus tuberomammillaris tend to collect in groups of varying density so that an estimate of the cell loss in these nuclei may be subject to an error of perhaps 10 or 15 per cent in some cases. The method used to estimate the amount of cell loss in the pathologic brains was to count the cells in a number of microscopic fields and compare this count with that made as nearly as possible in the same location in a normal brain. From these figures the total loss of nerve cells in a given nucleus was estimated on the percentage basis.

An attempt has been made also to evaluate the degenerative processes going on actively at the time of death. The percentage of cells in each nucleus which show definite chromatolysis has been estimated with a fair degree of accuracy, about the only basis for error in this case being the difficulty of establishing the borderline between a normal and a chromatolytic cell. Note has been made of any characteristics which might be taken to indicate whether the cell degeneration was mild or severe, recent or of long-standing, and whether gradual or erratic. The presence or absence of neuronophagia and any increase in the number of glia cells have been noted as indicative of the part these cells may be playing in the degenerative processes.

In addition to the points mentioned, general features, such as localized hyperemia, shrinkage, etc., have been noted. The condition of the basal optic ganglia and the paraventricular nucleus has been described briefly in some cases because of their close proximity to the other nuclei of the infundibular region and because the former nucleus is said by

Greving,[5] Pines[6] and Stengel[7] to send fibers to the hypophysis. Adjacent areas of the thalamus, subthalamus and corpus striatum have been examined as a matter of routine to make sure that the changes described for the nuclei of the infundibular region are not general throughout this entire area. The condition of the ventricles has been noted in order to ascertain that the localized distention of the third ventricle in the infundibular region could in no case be attributed to intraventricular pressure.

NORMAL HISTOLOGY

Since, with one exception, the gray matter of the third ventricle is not dealt with in textbooks of histology and neurology in this country, and some of the best literature on this subject is not readily available, it seems advisable to describe briefly the histology of the region of the tuber cinereum.

Malone[8] first gave an adequate description of this region in the human brain in 1910. In a recent paper, Malone[9] has enlarged on his original work. More recent work of other authors agrees, for the most part, with that of Malone (Spiegel and Zweig[10] and Greving[11] on the human brain, Friedemann[12] on the monkey, and others). The work of Grieving has been found especially valuable by me. The contributions of Malone will be taken as a basis for the following description. Three figures from his early work are reproduced in this paper (figs. 1, 2 and 3).

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5. Greving, R.: Beiträge zur Anatomie der Hypophyse und deren Funktion: II. Das nervöse Regulationssystem des Hypophysenhinterlappens, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:466, 1926.

6. Pines, J.: Ueber die Innervation der Hypophysis cerebri, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:123, 1925.

7. Stengel, E.: Ueber den Ursprung der Nervenfasern der Neurohypophyse in Zwischenhirn, Arb. a. d. neurol. Inst. d. Wien. Univ. **28**:25, 1926.

8. Malone, E. F.: Ueber die Kerne des menschlichen Diencephalon, Abhandl. d. k. preuss. Akad. d. Wissensch., suppl., 1910.

9. Malone, E. F.: The Nuclei tuberis lateralis and the So-called Ganglion Opticum basale, Johns Hopkins Hosp. Rep., 1914, Monograph no. 6.

10. Spiegel and Zweig: Zur Cytoarchitektonik des Tuber cinereum, Arb. a. d. neurol. Inst. d. Wien. Univ. **22**:278, 1919.

11. Greving, R.: Zur Anatomie, Physiologie und Pathologie der vegetativen Zentren im Zwischenhirn, Ergebn. d. Anat. u. Entwcklngsgesch. **24**:348, 1923; Beiträge zur Anatomie des Zwischenhirns und seiner Funktion, Ztschr. f. d. ges. Neurol. u. Psychiat. **99**:231, 1925.

12. Friedemann, M.: Die Cytoarchitektonik des Zwischenhirns des Cercopitheken mit besonderer Berücksichtigung des Thalamus opticus, Jahrb. f. Psychol. u. Neurol. **18**:309, 1911.

The Ganglion Opticum Basale (Nucleus Supra-Opticus of Greving).—This nucleus consists of a main mass of cells (fig. 1, *g.o.b.*) beginning in the anterior perforated substance and extending back along the lateral side of the optic tract. A second and smaller group of cells running parallel to the first group lies on the medial side of the optic tract. A third mass of more scattered cells extends over the optic tract, joining the other two groups. This nucleus is made up of large polygonal cells with very coarse processes. The nissl substance is collected in large masses which are concentrated at the periphery of the cell.

The Nucleus Paraventricularis Hypothalami.—This nucleus consists of an elongated, closely packed group of cells found at a level between the anterior

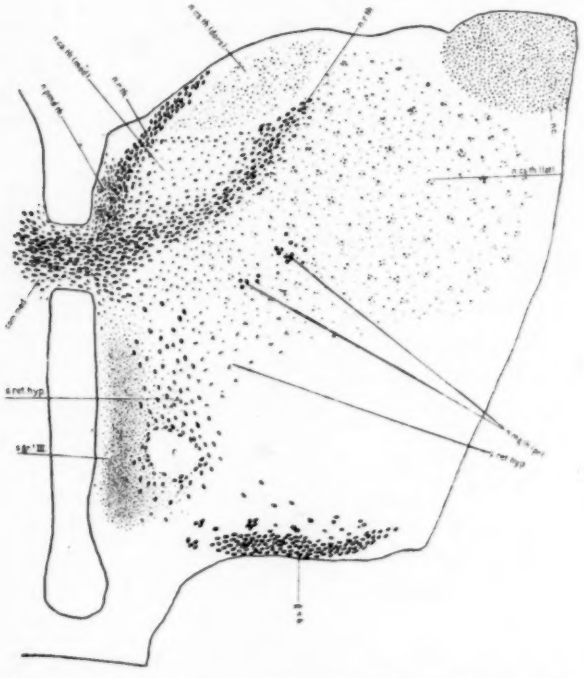

Fig. 1.—Diagram illustrating the nuclei of the diencephalon at the level of the optic chiasm (Malone); *g.o.b.* indicates the basal optic ganglion; *s.gr.III*, substantia grisea of the third ventricle; *f.*, fornix; *s.ret.hyp.*, substania reticularis hypothalami. The remaining nuclei make up the thalamus.

commissure and the optic chiasm. The nucleus lies close to the third ventricle, with its long axis perpendicular to the base of the brain and its lower end coming into close proximity to the oral end of the ganglion opticum basale. The cells of these two nuclei are very similar, differing chiefly in that the nissl substance in the cells of the paraventricular nucleus is collected in smaller masses and is more scattered through the cytoplasm.

The Nucleus Tuberis Lateralis.—In his earlier work Malone called this the nucleus tuberis. Later, however, he suggested changing this name to nucleus

tuberis lateralis because various authors have applied the former term to different structures in the region of the tuber so that the name is confusing. The nucleus tuberis lateralis consists of several groups of cells, more or less closely associated and embedded in the lateral or basilar portion of the tuber cinereum (fig. 2, *n.tb.*). These cell groups are well circumscribed in the human brain and have a characteristic appearance in the stained preparation, which makes them easily distinguishable from the surrounding areas even under very low magnification. The nucleus begins slightly caudal to the optic chiasm and extends to the anterior level of the mammillary body. The more expanded part of the nucleus is embedded in the area ventromedial to the cerebral peduncle. Extending medially, the cell masses become gradually more compressed against the base of the brain. The cells of the nucleus tuberis lateralis are considerably smaller than those of the

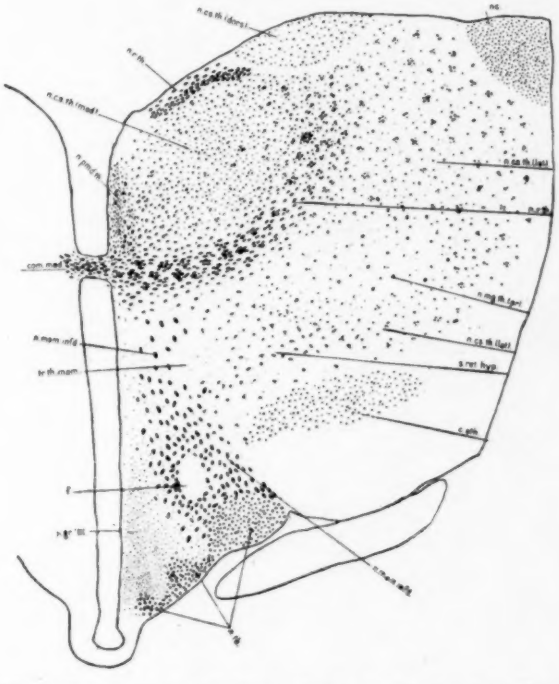

Fig. 2.—The cell groups in the diencephalon at the level of the infundibulum (Malone); *n.tb.* indicates the nucleus tuberis lateralis; *s.gr.III*, substantia grisea of the third ventricle; *f.*, fornix; *n.mam.infd.*, nucleus tuberomammillaris; *c.sth.*, subthalamic nucleus of Luys; *s.ret.hyp.*, substantia reticularis hypothalami (nucleus of Forel's field); *tr.th.mam.*, mammillothalamic tract; *com.med.*, intermediate commissure of the thalamus. The remaining nuclei belong to the thalamus and striatum (*nc*).

ganglion opticum basale, nucleus paraventricularis or nucleus tuberomammillaris, but are slightly larger than those of the substantia grisea (fig. 4, *3A*). These cells have a relatively small nucleus with a large amount of cytoplasm. The nissl substance exists as small granules, evenly distributed throughout the cytoplasm and

not taking a heavy nissl stain. This is in contrast to the larger nucleus, smaller amount of cytoplasm and coarser granules of the cells of the substantia grisea.

The Substantia Grisea Ventriculi Tertii.—This cell mass is bounded medially by the third ventricle. Laterally, the cells extend in some places beyond the fornix where they mingle freely with the cells of the nucleus tuberomammillaris. The nucleus extends from the thalamus to the base of the tuber and from the optic chiasm to the mammillary body (figs. 1, 2, 3, *S.gr.III*). The substantia grisea is composed of small cells with relatively large nuclei and a small amount of cytoplasm (fig. 4, *1*). Fairly coarse granules and small masses of nissl substance are scattered through the cytoplasm. There is considerable variation in the size of

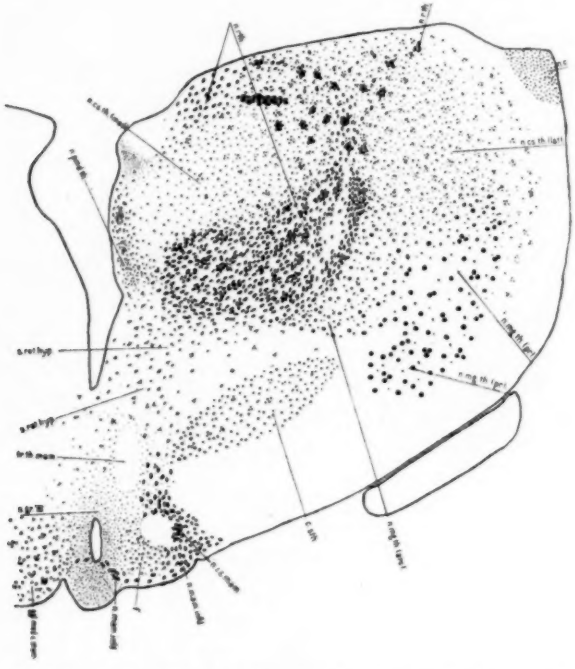

Fig. 3.—Nuclei of the diencephalon at the level of the mammillary bodies (Malone); *n.i.c.mam.* indicates the internal nucleus of the mammillary body. See also figure 2.

the cells in the substantia grisea. In general, the very small cells are more concentrated in the immediate vicinity of the third ventricle, where many larger cells are also present. In the more lateral part of the nucleus, especially in a large area ventral to the fornix, the cells are predominantly of the larger type. This difference in size of the cells gives the impression that the cells are more densely packed in the lateral part of the nucleus, while a cell count shows the opposite to be true.

The Nucleus Tuberomammillaris.—Malone, in his early work, called this the nucleus mammillo-infundibularis, and that term is used by Greving. Malone later pointed out that the term mammillo-infundibularis is misleading since this nucleus does not extend into the infundibulum, and suggested that tuberomammillaris is

a more appropriate name. The nucleus tuberomammillaris begins at the oral level of the optic chiasm and extends past the oral half of the mammillary body (figs. 2, 3 *N. mam. infd.*). At the lower level the nucleus is sometimes designated as the lateral ganglion of the mammillary body. At the higher level the cells are

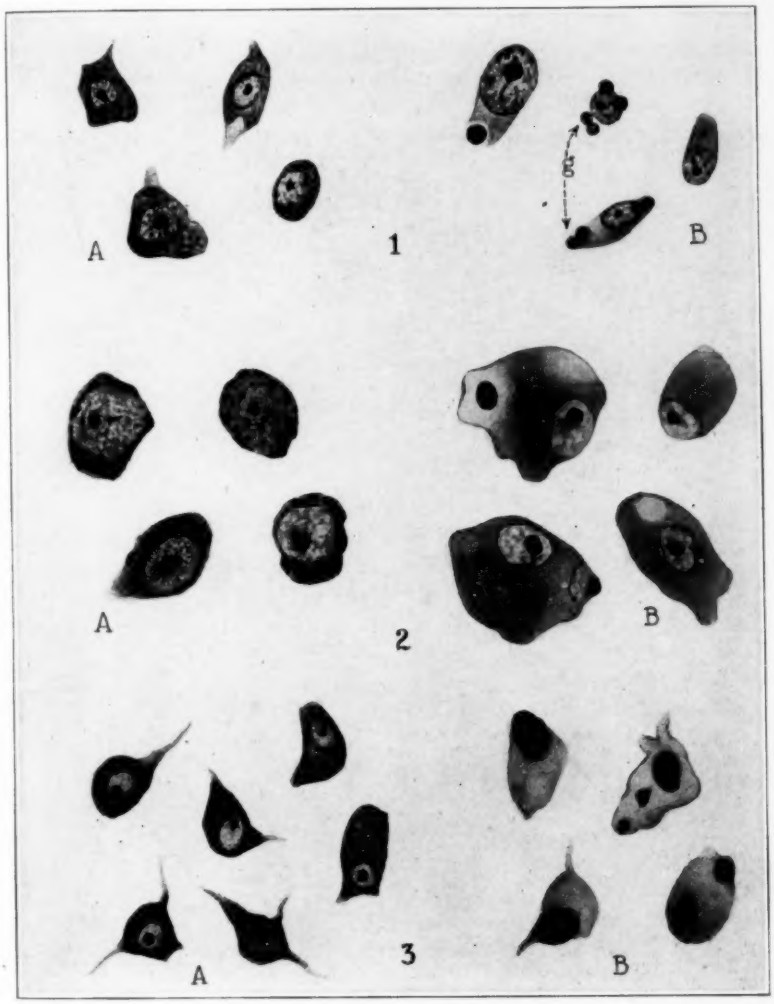

Fig. 4.—Drawing showing the cells of the nuclei of the tuber cinereum: 1 indicates the substantia grisea of the third ventricle; 2, nucleus tuberomammillaris; 3, nucleus tuberis lateralis; *A*, normal cells; *B*, degenerating cells from an epileptic brain (case 5); *g.*, glia cells.

concentrated around the fornix, particularly its lateral aspect, and some cells are scattered through the surrounding areas. At the level of the infundibulum the cells are greatly increased in number. There is an area of rather closely packed

cells around the fornix and extending laterally over the dorsal surface of the nucleus tuberis lateralis. A field of scattered cells extends cephalodorsad, being particularly concentrated in an area medial to the mammillothalamic fasciculus and Forel's field. Proceeding caudad, these cells become still more closely grouped about the fornix. At the oral level of the mammillary body the cells of the nucleus tuberomammillaris are grouped in an area ventrolateral to that structure. The nucleus tuberomammillaris is composed of large cells (fig. 4, *2*) slightly smaller than those of the basal optic ganglion which they somewhat resemble. Aside from being smaller, the nissl substance is less in amount and collected into

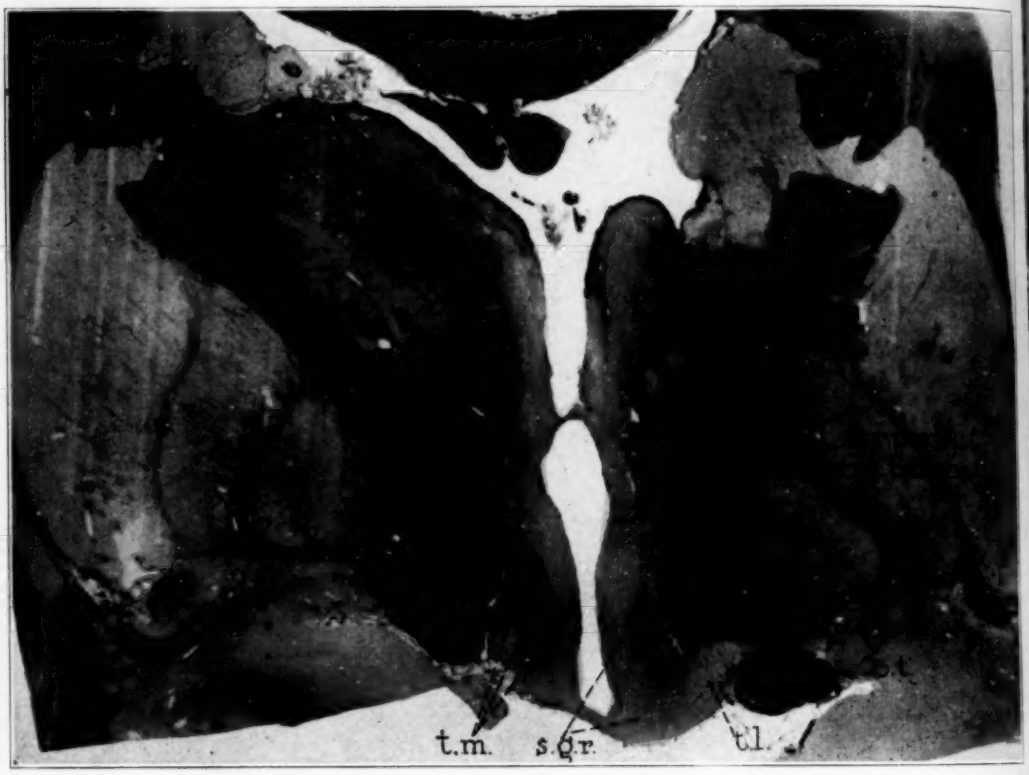

Fig. 5.—Section through the region of the infundibulum in a normal brain; *t.m.* indicates the nucleus tuberomammillaris; *s.gr.*, substantia grisea of the third ventricle; *t.l.*, nucleus tuberis lateralis; *o.t.*, optic tract; *f.*, fornix.

smaller masses. These masses of chromatin material, however, are usually located at the periphery of the cell. The nuclei are comparatively small, with frequently an indistinct nuclear membrane.

Malone concluded that the basal optic ganglion is phylogenetically the older of the nuclei described and is the most highly developed. The nucleus paraventricularis is next in order in these respects. The nucleus tuberomammillaris is less highly developed than either of these. The

nucleus tuberis lateralis is the most recent in origin of the nuclei under consideration. According to Malone, this nucleus is well defined in man, less so in *Macacus rhesus,* barely discernible in the lemur and absent in the cat. The substantia grisea of the third ventricle is an old nucleus, but is not highly developed. Its cells, especially the smaller ones, are closely related to the embryonic type of cell.

I believe that a nucleus tuberis lateralis or its equivalent is present in the dog and rat, although not present in the form of definitely circumscribed cell groups as it is in man. An examination of Dr. Coghill's collection of rat embryos at the Wistar Institute showed, in the late embryo and newly born, cell groups closely resembling the nucleus tuberis in man. In later growth, however, these cells become intermingled with those of the substantia grisea so as to make their identification very difficult.

The evidence available indicates that the nuclei of the tuber cinereum region receive fibers from the corpus striatum and probably from the cerebral peduncle. These fiber connections place these nuclei under the direct influence of both the corpus striatum and the cerebral cortex. The importance of this relationship will be emphasized in the later discussion. Little is known concerning the efferent fiber connections of the hypothalamic nuclei. According to Greving,[5] Pines[6] and Stengel,[7] the basal optic ganglion (nucleus supra-opticus) sends fibers to the hypophysis.

DESCRIPTION OF MATERIAL

CASE 1.—*History.*—Harry S. was admitted to the Craig Colony in 1921, at the age of 10 years. He was normal at birth; dentition began at 5 months, and he walked and talked at the age of 14 months, although he never got beyond saying a few words. No history of any nervous or mental disorder in the family was obtained. The onset of epilepsy was said to have occurred at the age of 3½ years. The patient never attended school, but was considered normal up to the onset of epilepsy. At the time of the first seizure he was said to have fallen from a small table, although no one observed the fall; he was found lying on his back on the floor. This fall was followed by considerable vomiting, but it was about two months before the first convulsion occurred. For six months the seizures recurred daily and then decreased in frequency until his admission to the colony, when they were occurring about once a month. The right hand was first affected and there was no apparent aura.

Examination.—When admitted to the colony he was a mentally defective, poorly nourished boy with an idiotic expression. The pupils were equal and normal in their reaction to light. The tongue was broad and thick. There was moderate cyanosis of the hands and feet. Examination of the chest and abdomen gave negative results. There was no paralysis. The reflexes were normal. There was an unsteady gait due apparently to poor coordination. He was classified mentally as an idiot.

Course.—In January, 1922, diarrhea developed; a few days later there was a left parotitis, which was incised; a thick pus exuded. The temperature dropped to normal a few days later, but the patient failed and died on February 4.

During 1921, twenty-six seizures were recorded, although he probably had a greater number which were not observed by the nurses or attendants in charge.

Necropsy.—Postmortem examination showed an emaciated white boy, poorly developed, with flabby musculature. The heart, lungs, thyroid, liver and kidneys were normal. The suprarenals were small and somewhat fibrous. There was some thickening of the dura, with slight congestion of the pia and arachnoid. The brain weighed 1,375 Gm., was microgyric and of rather firm consistency. There was no apparent abnormality of either the pituitary or pineal gland. There was marked necrosis of the left parotid gland. A culture from the gland and from the heart blood showed *Streptococcus hemolyticus.* The cause of death was given as *Streptococcus hemolyticus* septicemia following suppurative parotitis. The brain was sent by Dr. Shanahan to Dr. G. B. Hassin, from whom it was obtained for microscopic examination.

Microscopic Examination.—There was a pronounced hyperemia throughout the thalamic, subthalamic and striate areas. There was marked shrinkage in the walls of the third ventricle in the subthalamic and infundibular regions.

Left Side: There was almost complete destruction of about one half of the substantia grisea of the third ventricle comprising the medial and basilar portions. Throughout the remainder of the nucleus, the cells were reduced to about one half the normal number. Eighty per cent of the remaining cells showed chromatolysis, over half of which was in the more advanced stages. Many cells were in the final stages of degeneration. Neuronophagia was common. The glia cells were nearly three times the number found in the normal brain.

The nucleus tuberomammillaris showed a loss of well over half its cells. Eighty-five per cent of the remaining cells were chromatolytic. The majority of the cell degeneration was in the advanced stages, with occasional neuronophagia.

There was a loss of from 60 to 70 per cent of the cells of the nucleus tuberis lateralis. Over 90 per cent of the remaining cells were chromatolytic. In most of these cells the cytoplasm had been completely dissolved away from around the nucleus, and groups of glia cells frequently were seen lying in the cytoplasmic space. There was a slight increase in glia cells above the normal number.

There was chromatolysis of about 55 per cent of the cells of the basal optic ganglia. This chromatolysis was almost entirely in the early stages and there was no apparent cell loss.

Twenty per cent of the cells of the peripeduncular nucleus showed a mild degree of chromatolysis.

Right Side: This half of the brain stem was cut in the sagittal plane so that a direct comparison could not be made with the normal. A careful study of the sections, however, indicated that the same changes were present on this side as were described for the left side of the brain. In fact, the destruction seemed to be even greater than that described.

Case 2.—*History.*—Anna H., a white woman, a seamstress, was admitted to Craig Colony in 1896 at the age of 25 years. Epilepsy was said to have begun at the age of 14 years. The seizures were irregular in occurrence and of grand mal type. Later, information was obtained which indicated that when the patient was 10 years of age she had convulsions following a severe blow in the epigastrium. These seizures recurred, and then there was a remission until the age of 14 years. There was a history of some mental impairment with periods of depression, and at one time suicide was attempted. Memory was poor, and at times the patient was excited in postepileptic delirium.

Examination.—When admitted to the colony, the patient was anemic and in a poor physical condition. The pupils were normal. Speech was nasal, drawling and monotonous. There was a marked bromide acne. The deep reflexes were exaggerated.

Course.—During residence at the colony she had frequent periods of excitement during which hallucinations and delusions were well marked. Seizures while at the colony were mostly of grand mal type, averaging from two to six a month. The patient died on Feb. 24, 1922, of lobar pneumonia.

Necropsy.—Examination confirmed the clinical diagnosis. The heart was conspicuously dilated, with evidence of myocarditis. There were atheroma of the

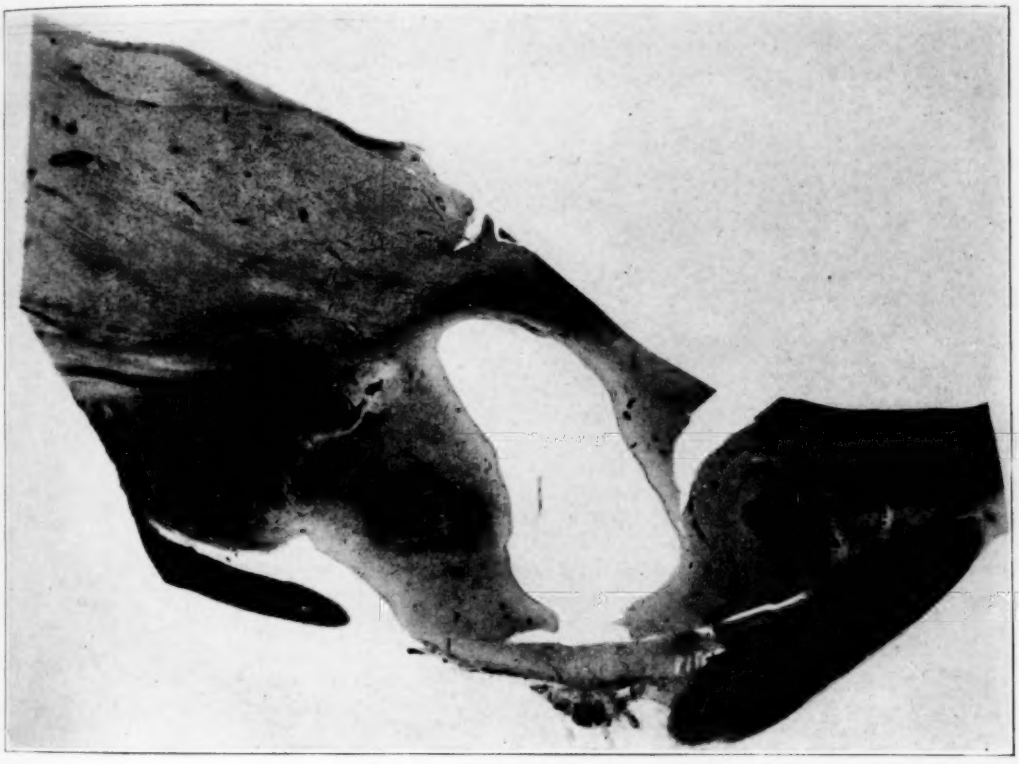

Fig. 6.—Section through the infundibular region of the brain in case 2; compare with figure 5.

descending aorta, chronic nephritis and a small persistent thymus. The cerebral blood vessels were congested. Through the courtesy of Drs. Shanahan and Hassin this brain was obtained for study.

Microscopic Examination.—There was a pronounced hyperemia in the area between the cerebral peduncles and the basal part of the third ventricle. There was marked distention of that portion of the ventricle that lies below the intermediate commissure of the thalamus, owing to a shrinkage of the adjacent tissues. The width of the ventricle in the infundibular region (fig. 6) was ten times that of the normal brain.

Right Side: Great shrinkage was evident in the area occupied by the substantia grisea of the third ventricle. There was almost total destruction of the cells in a narrow zone adjoining the third ventricle and in the basal infundibular portion of the nucleus. These areas of total destruction comprised about one half of the total area occupied by the substantia grisea. The cells in the remainder of the nucleus were reduced to about 30 per cent of the normal. About 85 per cent of these cells showed chromatolysis which was generally distributed through all stages. Many cells were in the final stages of degeneration, with frequent neuronophagia. The glia cells were more than double the number found in the normal brain.

The nucleus tuberomammillaris showed a cell reduction of approximately 50 per cent. Over 75 per cent of the remaining cells showed chromatolysis, which was about equally distributed through all stages. Many cells were in the final stages of degeneration, with frequent neuronophagia. The dorsal part of the nucleus was more affected than the ventral.

The cells of the nucleus tuberis lateralis were reduced to less than 25 per cent of the normal number. There was chromatolysis of more than 90 per cent of the remaining cells. Most of the cells were in the final stages of degeneration, with frequent neuronophagia.

About 15 per cent of the cells of the basal optic ganglia were in the earliest stages of chromatolysis. No cell loss was evident.

Left Side: There was much shrinkage in the area occupied by the substantia grisea of the third ventricle. There was almost complete destruction of the medial and basal part of the nucleus involving over one third of the whole. The cells in the remainder of the nucleus were reduced to less than 25 per cent of the normal number. Eighty-five per cent of the remaining cells were chromatolytic. All stages of chromatolysis were well represented, with many cells in the final stages of degeneration. Neuronophagia was common. The glia cells were nearly three times the number found in the normal brain.

A small amount of cell loss was evident in the nucleus tuberomammillaris. This cell loss probably did not exceed 25 per cent. About 75 per cent of the remaining cells were chromatolytic. All stages of chromatolysis were well represented, many cells being in the final stages of degeneration. Neuronophagia was common. The dorsal part of the nucleus was most affected.

There was marked shrinkage in the nucleus tuberis lateralis. The cells were reduced to about 25 per cent of the normal number. Ninety per cent of the remaining cells were chromatolytic. Most of these were in the final stages of degeneration. Neuronophagia was well in evidence. Approximately the normal number of glia cells were present.

The basal optic ganglion was normal.

Case 3.—(This brain as well as the case history were obtained through Dr. M. T. Koenig of the Elgin State Hospital.) *History.*—John R., a white man, was said to have had convulsions since the age of 5 years. He had been treated with bromides, but without success. He entered the Elgin (Ill.) State Hospital on Aug. 8, 1927, at the age of 23 years.

Physical Examination.—When admitted he was poorly nourished, with pale sallow skin and coarse hair. He was in a stuporous condition, did not talk and did not seem to understand when spoken to. The blood pressure was 100 systolic and 80 diastolic. The pupils were equal and reacted to light. He was extremely rigid. The face was set, the knee reflexes were much exaggerated and ankle clonus was present, but the Babinski sign was negative. Any effort to produce a movement of any duration was accompanied by clonic tremor of the entire body.

Course.—Death occurred about two and a half months after admission to the hospital. The patient had several seizures while under observation. The rigidity was general and constant. During the last few days of life the patient became unconscious, convulsions occurring from five to eight times a day.

On August 17, the blood gave a 4 plus Wassermann reaction and a 1 plus Kahn reaction. On August 29, the blood gave a negative Wassermann, and an unsatisfactory Kahn reaction. The cerebrospinal fluid gave negative results with the Wassermann and Kahn tests.

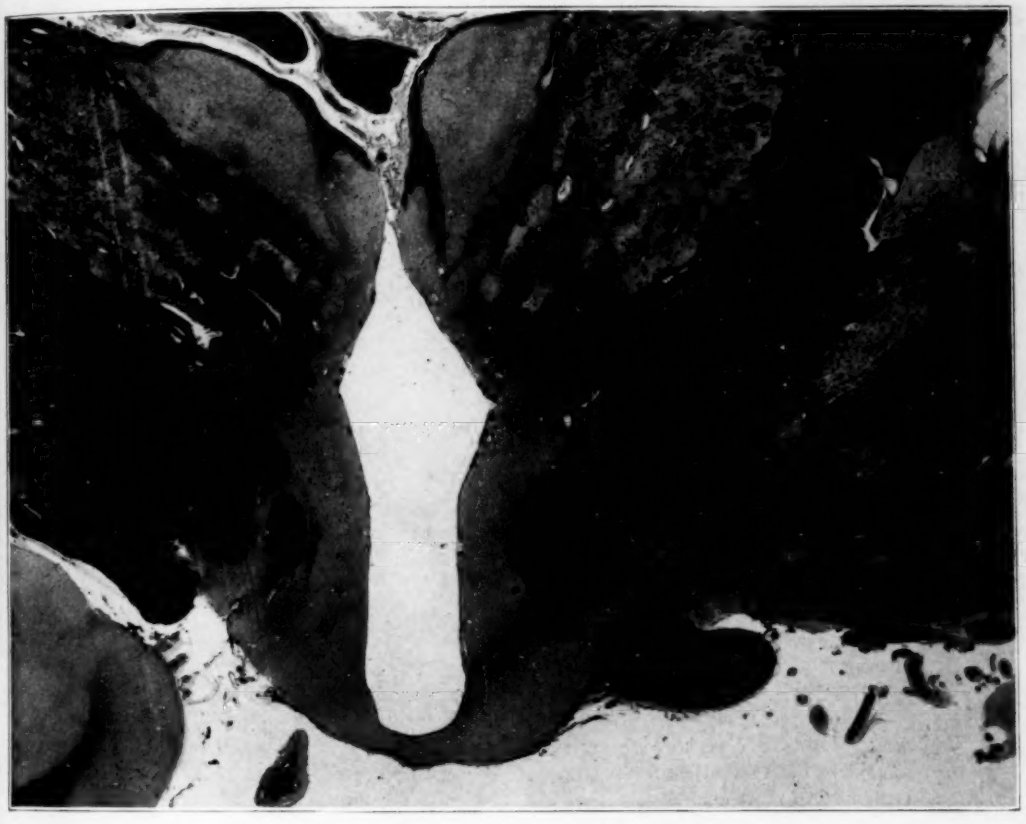

Fig. 7 (case 3).—Compare with figure 5.

Microscopic Examination of the Brain.—There was a marked localized distention of the third ventricle in the subthalamic and infundibular region, due to a shrinkage of adjacent tissues (fig. 7).

Left Side: There was generalized cell destruction throughout the substantia grisea of the third ventricle. The cells were reduced to less than 25 per cent of the normal number. Seventy per cent of the remaining cells showed chromatolysis, which was well distributed through all stages. Neuronophagia was common among the cells in the more advanced stages of degeneration. The glia cells were about double the normal number.

About 60 per cent of the cells of the nucleus tuberomammillaris were chromatolytic. More than half of this chromatolysis was in the earlier stages. Although some cells were in the final stages of degeneration with occasional neuronophagia, there was not sufficient cell loss to be readily perceptible.

There was about 70 per cent cell loss in the nucleus tuberis lateralis. The lateral portion of the nucleus was more affected than the rest. About 90 per cent of the remaining cells were chromatolytic. Most of these cells were in the final stages of degeneration with frequent neuronophagia. The glia cells were about double the normal number.

Right Side: The cells of the substantia grisea of the third ventricle were reduced to about 16 per cent of the normal number. There was chromatolysis in about 85 per cent of the remaining cells. About half of this was in the more advanced stages, with frequent neuronophagia. The glia cells were more than double the normal number.

The dorsal part of the nucleus tuberomammillaris was most affected. Ninety-five per cent of the cells in the dorsal portion were chromatolytic as compared to 55 per cent in the ventral part. Many cells were in the final stages of degeneration. There was some reduction in the number of cells, amounting probably to not more than 20 per cent.

There was almost complete destruction of the nucleus tuberis lateralis. It was estimated that about 10 per cent of the cells remain and these were chromatolytic. The glia cells were increased somewhat in number.

Twelve per cent of the cells of the basal optic ganglion showed chromatolysis, which was almost entirely in the earliest stages. There was no evident cell loss.

Case 4.—*History.*—George H., a man, was said to have had convulsions since early childhood. The father and one brother had mental disease. A psychosis developed when the patient was 41 years of age. He was admitted to the Binghamton (N. Y.) State Hospital at the age of 42. He acted peculiarly, had suicidal and homicidal tendencies, with periods of religious exaltation. There were paranoid tendencies. The convulsions were frequent and grand mal in type. The seizures became gradually less frequent and disappeared entirely a few years before death. The mental deterioration continued to increase gradually. A diagnosis of epileptic psychosis was made.

The patient died on March 31, 1927, at the age of 73. The cause of death was general arteriosclerosis with gangrene of the left foot. Through Dr. H. S. Gregory the brain was obtained for study.

Microscopic Examination of the Brain.—There was marked hyperemia in the walls of the third ventricle, especially in the basilar part. The ventricle was distended in the region below the intermediate commissure of the thalamus. In the region of the infundibulum it was six times the normal width.

Left Side: There was almost complete destruction of cells in the basilar part of the substantia grisea and in a zone extending upward along the lateral side of the nucleus into the region of the fornix. In this lateral zone there were many remnants of degenerated nerve cells. In a medial zone adjacent to the ventricle the cells were reduced to 30 per cent of the normal number, nearly all of which were in the final stages of degeneration. In an intermediate area the cells were reduced to 43 per cent. The remaining cells were all chromatolytic. The majority of these were in the more advanced stages of chromatolysis, with frequent neuronophagia. It was estimated that for the entire nucleus there was a loss of 80 per cent of the nerve cells. The glia cells were double the normal number in the intermediate area, slightly increased in the lateral zone, but reduced in number in the remainder of the nucleus.

Eighty per cent of the cells of the nucleus tuberomammillaris showed chromatolysis. Most of this was in the early phases, but many cells reached the more advanced stages. Neuronophagia was rare. There was a total destruction of the cells ventral and medial to the fornix, considerable cell reduction in the dorsal part of the nucleus, and some in the remaining portion. For the entire nucleus there was probably a loss of 40 per cent of the cells.

There was a loss of approximately 10 per cent of the cells in the lateral one fifth of the nucleus tuberis lateralis. There was a loss of perhaps 65 per cent of the cells throughout the remainder of the nucleus. There was 80 per cent chromatolysis in the lateral part of the nucleus. This was equally distributed through all phases, frequently reaching the final stages of degeneration. Neuronophagia was common. There was no evident increase in the number of glia cells. The medial portion of the nucleus contained no perfectly normal cells, although many of them were not affected to a very great degree. There were here many cells in the more advanced stages of chromatolysis. There was frequent neuronophagia. The glia cells were 50 per cent more than the normal number.

Thirty-five per cent of the cells in the basal optic ganglion showed chromatolysis which seldom reached the advanced stages. No cell loss was evident.

The paraventricular nucleus showed changes similar to those in the basal optic ganglion.

Right Side: There was almost total loss of the nerve cells of the substantia grisea in its basilar part and in a narrow zone extending upward along the third ventricle. There was a general cell reduction in the remainder of the nucleus which amounted to about 50 per cent. For the entire nucleus it was estimated that there was a loss of over 65 per cent of the cells of the substantia grisea. Eighty per cent of the remaining cells showed chromatolysis, over half of which was in the later stages. Neuronophagia was frequent. The glia cells were about two and one half times the normal number.

There was considerable cell reduction in the dorsal part of the nucleus tuberomammillaris and a small amount in the ventral part. It was estimated that there was a total loss of 35 per cent of the cells in the entire nucleus. Eighty per cent of the remaining cells showed chromatolysis which was generally distributed through all phases with many cells in the final stages of degeneration. There was occasional neuronophagia.

There was practically total destruction of the nerve cells in the medial part of the nucleus tuberis lateralis. There was a loss of 75 per cent or more of the cells in the intermediate portion, with nearly all the remaining cells in the final stages of degeneration. The lateral part of the nucleus showed a loss of probably 40 per cent or more of its cells. Ninety-five per cent of the remaining cells were chromatolytic. The large majority of these were in the final stages of chromatolysis. Neuronophagia was very common. The glia cells were nearly double the normal number.

Thirty per cent of the cells of the basal optic ganglion were in the early stages of chromatolysis. There was no cell loss.

The brains studied in cases 5 and 6 were shipped to Dr. Hassin from the Massachusetts State Hospital for Epileptics. The records accompanying the specimens state that they were from bona fide epileptic patients. Unfortunately, I have been unable to secure case histories of these patients.

CASE 5.—*Microscopic Examination of the Brain.*—There was marked localized distention of that portion of the third ventricle which lies below the intermediate commissure of the thalamus (fig. 8). The ventricle in the infundibular region was about seven times the normal width. There was very marked hyperemia confined to the wall of the third ventricle, especially in the more basilar portion.

Right Side: The cells of the basilar portion of the substantia grisea of the third ventricle, which extends into the infundibular region, were completely destroyed. This area constituted perhaps a fifth of the entire nucleus. In the remainder of the nucleus the cells were reduced to 40 per cent of the normal in the medial portion and to less than 25 per cent of the normal number in the

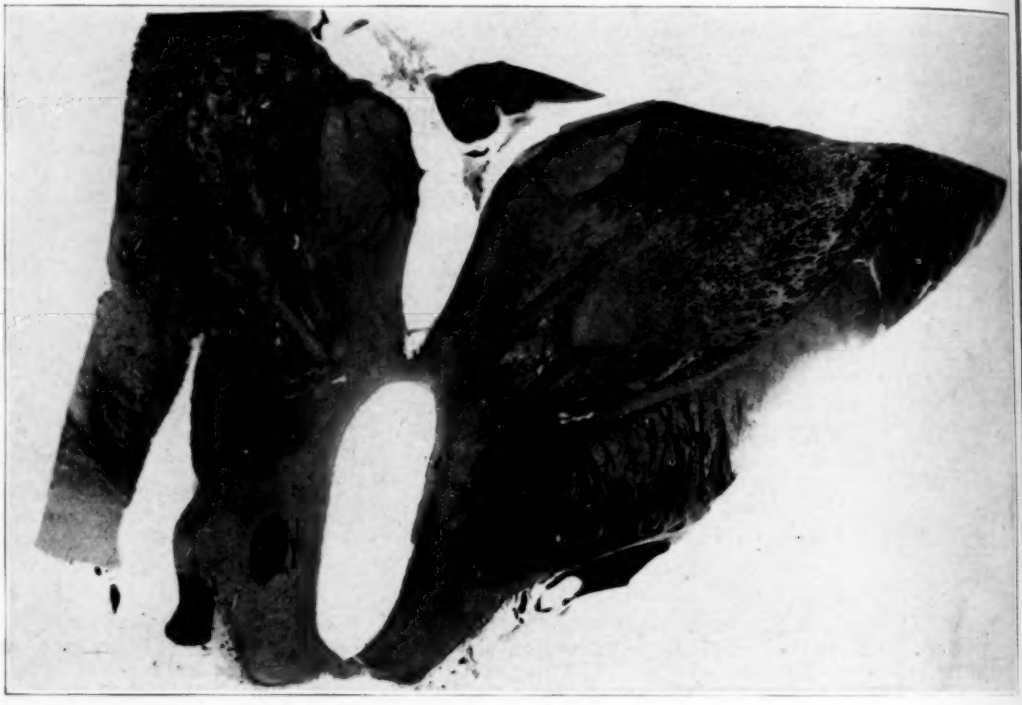

Fig. 8 (case 5).—Compare with figure 5.

lateral portion. So for the entire substantia grisea there was an estimated loss of 75 per cent of the cells. Eighty-five per cent of the remaining cells showed chromatolysis. The majority of this was in the late stages, with frequent neuronophagia. The glia cells in the area containing nerve cells were increased to more than three times the normal, while in the area where there was total destruction of nerve cells the glia cells were reduced in number.

There was a loss of probably 25 per cent of the cells of the nucleus tuberomammillaris. Eighty-two per cent of the remaining cells were chromatolytic. Over half of these were in the more advanced stages of degeneration. Neuronophagia was common.

There was marked shrinkage in the region occupied by the nucleus tuberis lateralis. There was almost total destruction of the medial division of this

nucleus. The few remaining cells were in the final stages of degeneration. Degeneration became progressively less toward the lateral side of the nucleus. In the lateral two thirds of the nucleus there was a loss of at least 25 per cent of the cells. It was estimated that for the entire nucleus there was a loss of about 45 per cent of the cells. Over 75 per cent of the cells in the lateral two thirds of the nucleus were chromatolytic. The majority of this chromatolysis was in the more advanced stages, with occasional neuronophagia. The glia cells were nearly double the normal number.

Left Side: There was a complete destruction of the cells in the basilar portion of the substantia grisea in the region of the infundibulum. In a zone from 1 to 2 mm. in width, immediately adjacent to the ventricle, the cells were reduced to 10 per cent of the normal number. In the remainder of the nucleus the cells were reduced to about 40 per cent of the normal. On the whole, then, there was a total cell loss of about 80 per cent for the substantia grisea of the third ventricle. The remaining cells showed over 80 per cent chromatolysis, evenly distributed through all stages, with frequent neuronophagia in the later phases. In the more lateral area where the cell destruction was least the glia cells were more than three times the normal number. In the medial zone there were four times the normal number of glia cells, while there was a reduction in the number of glia in the basilar portion where the cell destruction was complete.

In the nucleus tuberomammillaris there was almost complete destruction of the cells lying ventral, medial and lateral to the fornix. There was some cell reduction in the remainder of the nucleus. In all, the cells of this nucleus were reduced to perhaps 40 per cent or less of the normal number. Seventy-five per cent of the remaining cells were chromatolytic. Many of these were in the later stages of degeneration, with frequent neuronophagia.

There was marked shrinkage in the nucleus tuberis lateralis. There was almost total destruction of the cells in the medial division of the nucleus with the remaining cells in the final stages of degeneration. The intermediate portion showed about 70 per cent cell loss while the cells in the lateral part were reduced about 50 per cent in number. This made for the entire nucleus a loss of approximately 70 per cent of the cells. All of the remaining cells in the intermediate portion and 85 per cent of those in the lateral part were chromatolytic. The large majority of this chromatolysis was in the more advanced stages, with frequent neuronophagia. There was no increase in the number of glia cells in the areas in which cell destruction was complete, but the remaining areas showed double the normal of glia cells.

Sixty-five per cent of the cells of the basal optic ganglion showed chromatolysis. This very seldom reached the more advanced stages. Neuronophagia was rare. There was slight cell loss, if any.

About 22 per cent of the cells of the peripeduncular nucleus showed a mild degree of chromatolysis. There was no evident cell loss.

CASE 6.—*Microscopic Examination of the Brain.*—There was very pronounced hyperemia in a zone immediately adjoining the third ventricle in the subthalamic and infundibular regions. Shrinkage in this same area caused the third ventricle to be distended to about six times its normal width (fig. 9).

Left Side: There was great shrinkage in the area occupied by the substantia grisea of the third ventricle. There was almost complete destruction of the basilar portion of this nucleus as well as a zone, 1 mm. in width, adjacent to the ventricle. In the remaining three fifths of the nucleus the cells were reduced to 50 per cent of the normal number. Eighty-five per cent of the remaining cells showed chromatolysis. The majority of this was in the most advanced stages,

with frequent neuronophagia. The glia cells were multiplied nearly three times in the area in which active degeneration was in progress.

The nucleus tuberomammillaris showed about 50 per cent chromatolysis which was fairly equally distributed through all stages, with frequent neuronophagia. A small amount of cell reduction was evident in the ventral part of the nucleus.

Ninety per cent of the cells of the nucleus tuberis lateralis were chromatolytic. Over half of the chromatolysis was in the later stages with many cells in the final stages of degeneration. There was frequent neuronophagia. The glia cells were more than double the normal number. There was an estimated loss of at least 30 per cent of the cells in this nucleus.

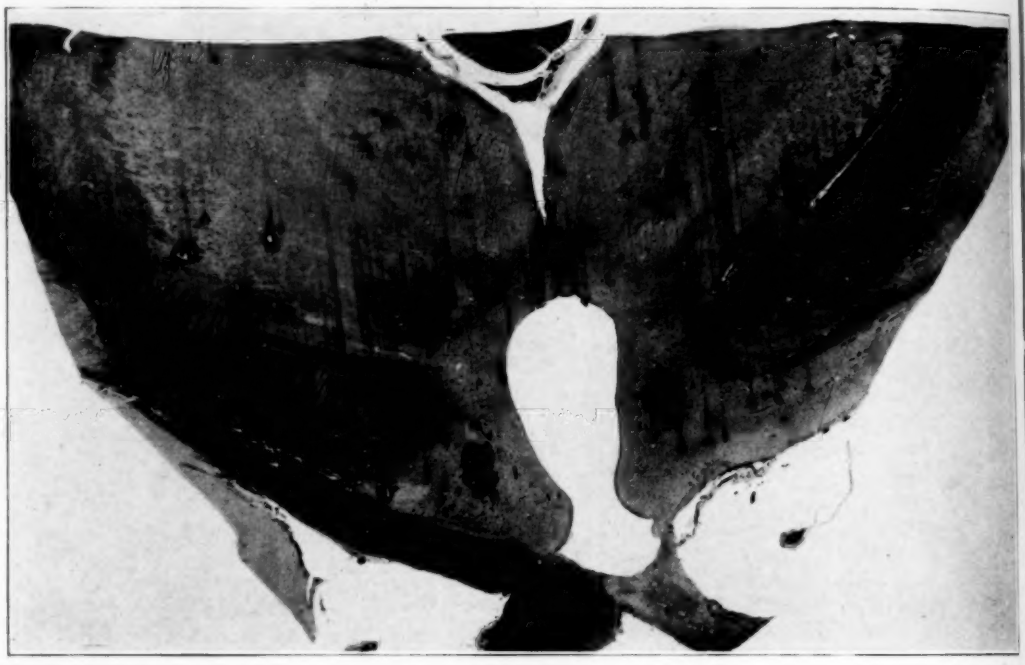

Fig. 9 (case 6).—Compare with figure 5.

Right Side: There was almost total destruction of about three fifths of the substantia grisea, including the basilar portion and a zone, 1 mm. in width, extending along the ventricle. Cell reduction became progressively less in the deeper parts of the nucleus. In this area it was estimated that there was a loss of 60 per cent of the cells. Eighty per cent of the remaining cells were chromatolytic. All stages of chromatolysis were well represented, with frequent neuronophagia in the later stages. The glia cells were more than double the normal number.

Eighty per cent of the cells of the nucleus tuberomammillaris showed chromatolysis which was pretty equally distributed through all stages. Neuronophagia was frequent among the cells which were in the more advanced stages of chromatolysis. Cell reduction was evident, especially in the anterior and basilar part. It was estimated that there was a destruction of 40 per cent or more of the cells in this nucleus.

There was a loss of 75 per cent of the cells in the nucleus tuberis lateralis in its medial part and a loss of 20 per cent or more in the more lateral portion. Over 90 per cent of the remaining cells showed chromatolysis. This chromatolysis was nearly all in the later stages in the more medial portion of the nucleus, while in the lateral part it was about equally distributed through all phases. There was very active neuronophagia in the medial part of the nucleus with a moderate amount in the lateral portion. Likewise, the glia cells were increased about six times in the medial and were more than double the normal number in the lateral area.

Twelve per cent of the cells of the basal optic ganglion showed a mild degree of chromatolysis.

COMMENT

It is obviously impossible to review adequately the literature on all the topics touched on in this discussion. The pathologic and clinical observations in epilepsy, are generally known and have been frequently reviewed (Reichardt, Wuth, Spielmeyer and Rudin,[13] Notkin,[14] Altschul,[15] Mott,[16] Schröder,[17] Gruhle,[18] and others). I am primarily interested in the function of the nuclei in the region of the tuber cinereum and their relation to diseases of the nervous system. Some of the literature dealing with that phase of the problem will be considered.

There is considerable evidence to support the view that there is a center in the region of the tuber cinereum which has a profound influence on the regulation of body temperature (Jakoby and Roemer,[19] Walbaum,[20] Isenschmid and Schnitzler,[21] Reichardt,[22] Glaser[23] and

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21. Isenschmid, R., and Schnitzler, W.: Beitrag zur Lokalisation des Wärmeregulation vorstehenden Zentralapparates im Zwischenhirn, Arch. f. exper. Path. u. Pharmakol. **76**:202, 1914.

22. Reichardt, M.: Ueber die Störungen der Korpertemperature und der vasomotorischtrophischen Funktionen bei Hirnerkrankungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **18**:417, 1912.

23. Glaser, W.: Beitrag zur Kenntnis des cerebralen Fiebers, Ztschr. f. d. ges. Neurol. u. Psychiat. **17**:493, 1913.

others). Much of this evidence suggests that this center lies very close to the third ventricle. Three main factors are concerned with the regulation of the body temperature: (1) the rate of metabolism in the tissues; (2) the activity of the sweat glands and its influence on the rate of loss of heat from the body surface; (3) the dilatation and constriction of the peripheral blood vessels, which help to govern the amount of heat reaching the surface of the body to be eliminated. Among the investigations thus far carried out there is little to indicate what factor or group of factors are concerned with the regulation of body temperature by the centers in the tuber cinereum.

Karplus and Kreidl,[24] Gerstmann,[25] and Schrottenbach [26] located a vasomotor center in the medial region of the subthalamic nucleus of Luys. Later, Karplus and Kreidl [27] demonstrated a rise in blood pressure following stimulation in the region of the infundibulum in the cat. They found that this influence of the hypothalamus on blood pressure was retained after removal of the hypophysis and suprarenals. Nevertheless, these authors believed that a close relationship exists between the hypothalamus and the internal secreting glands. Claude and Lhermitte [28] described marked cardio-vascular irregularities in a case of tumor of the third ventricle.

According to some authors (Bechterew, Lichtenstern, and Karplus and Kreidl [29]) there is a center in the hypothalamus for the contraction of the bladder. Karplus and Kreidl placed this center in the subthalamic nucleus of Luys. Other authors (Ott, Ekhard, Affanasiew, Bechterew, Mislowski, and Aschner [29]) placed a center in the hypothalamus which is concerned with the contraction of the uterus and the gastro-intestinal canal.

Cushing,[30] Bell [31] and others have ascribed adiposogenital dystrophy and polyuria to disease or removal of the pituitary gland. Adiposogenital dystrophy has become pretty generally accepted as being related

24. Karplus, C., and Kreidl, A.: Gehirn und Sympathicus. IV. Mitteilung, Arch. f. d. ges. Physiol. **171**:192, 1918.

25. Gerstmann: Zur Frage der sympathischen Gehirnbahnen, Jahrb. f. Psychiat. u. Neurol. **34**:287, 1913.

26. Schrottenbach: Beiträge zur Kenntnis der Ueberträgung, vasovegetativer Funktionen im Zwischenhirn, Ztschr. f. d. ges. Neurol. u. Psychiat. **33**:229, 1916.

27. Karplus, J. P., and Kreidl, A.: Gehirn und Sympatheticus. VII Mitteilung, Arch. f. d. ges. Physiol. **215**:667, 1927.

28. Claude, H., and Lhermitte, J.: The Infundibular Syndrome in a Case of Tumor of the Third Ventricle, abstr., Endocrinology **4**:126, 1920.

29. Quoted by Greving.

30. Cushing, H.: The Pituitary Body, Philadelphia, J. B. Lippincott & Company, 1912.

31. Bell, William Blair: The Pituitary, New York, William Woods & Company, 1920.

to the pituitary gland (hypophysis.) However, there is much evidence to support the view that polyuria is a symptom of hypothalamic injury rather than being dependent on the pituitary (Aschner,[32] Houssay,[33] Leschke and Schneider,[34] Camus and Roussy,[35] Bailey and Bremer,[36] Sachs and Macdonald,[37] Smith,[38] and others). Aschner, Bailey and Bremer, Camus and Roussy, and Sachs and Macdonald noted that glycosuria sometimes followed injury to the hypothalamus. Camus and Roussy and Smith found that following injury to the tuber cinereum there developed adiposity and genital atrophy. Smith found that the typical adiposogenital syndrome of Fröhlich occurred after both removal of the hypophysis and injury to the tuber in young animals. Many clinical cases are on record which show the occurrence of adiposogenital dystrophy, polyuria and glycosuria following tumors, lesions or injury in the region of the hypophysis. As to the exact location of the structures responsible for these symptoms, however, the clinical evidence is very conflicting. The fiber connection between the basal optic ganglion (nucleus supra-opticus) and the hypophysis, described by Greving, Pines and Stengel, probably explains to some extent the confusion which exists in this region, and why injury to the hypophysis is frequently followed by symptoms which are similar if not identical with those following injury to the tuber region of the brain. Moreover, Collin[39] has produced evidence to show that the secretion from the hypophysis is poured into the third ventricle and exerts a marked influence on the centers which lie at the base of the brain. Raab[40] found that small doses of pituitary extract, when injected into the ventricle or larger doses, when injected hypodermically cause a decrease in the amount of fat in the blood. This reaction was eliminated by destroying the infundibulum and tuber, division of the cervical cord

32. Aschner, B.: Ueber die Funktion der Hypophyse, Arch. f. d. ges. Physiol. **146**:1, 1912.

33. Houssay: Compt. rend. Soc. de biol. **81**:381, 1918.

34. Leschke and Schneider: Einfluss des Zwischenhirns auf den Stoffwechsel, Verhandl. d. Kong. f. innere Med., 1920.

35. Camus, J. E., and Roussy, G.: Experimental Researches on the Pituitary Body, Endocrinology **4**:507, 1920.

36. Bailey, P., and Bremer, F.: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec.) 1921.

37. Sachs, E., and Macdonald, M. E.: Blood Sugar Studies in Experimental Pituitary and Hypothalamic Lesions, Arch. Neurol. & Psychiat. **13**:335 (March) 1925.

38. Smith, P. E.: The Disabilities Caused by Hypophysectomy and Their Repair, J. A. M. A. **88**:158 (Jan. 15) 1927.

39. Collin, R.: Sur les relations fontionnelles entre la glande pituitaire et les centres tuberiens, Ann. de méd. **18**:428, 1928.

40. Raab, W.: Beiträge zur Genese zentralnervös-bedingter Störungen des Fettstoffwechsels, Klin. Wchnschr. **5**:1516, 1926.

or sectioning of the splanchnic nerve. Another confusing factor is perhaps found in the great variety of methods that have been used in investigating this region. Electrical stimulation, mechanical injury, chemical lesions, tumors and pathologic lesions differ in the way in which they act on the tissues, and one might expect the tissues of the hypophysis as well as the adjacent nerve tissues to differ somewhat in the manner in which they react to these various injuries.

It will be observed, in summing up the more or less fragmentary knowledge gained from the literature, that certain definite indications are evident. The indications are that there are centers in the region of the tuber cinereum that exert a definite influence on the smooth musculature of the body (affecting the bladder, gastro-intestinal canal and cardiovascular activity), on heat regulation, and on carbohydrate, protein, and water metabolism.

It will be noted that in our experiments on these areas in the dog, practically all of the factors mentioned were combined in one definite syndrome which, with the addition of other symptoms, made up a typical epileptic fit. The epileptic fit as it occurred in these animals is divisible into at least two major syndromes. The first involves the involuntary nervous system and consists of increased salivation, dilatation of the pupils, vasoconstriction, increased heart rate, rise in blood pressure, erection of the penis, constriction of the bladder, and relaxation of the musculature of the gastro-intestinal canal. It will be observed that this same combination of symptoms is obtained with large injections of epinephrine. Furthermore, I have shown that these symptoms cease in the operated animal when the suprarenal glands are ligated. The second syndrome involves the voluntary musculature and constitutes the convulsions which are characteristic of epilepsy. I have shown that these muscular spasms cease with the ligation of the thyroid and parathyroid glands. Whether one or both of these glands are responsible for this symptom has not been ascertained. The temperature of the animal increased in direct proportion to the frequency and severity of the muscular spasms and is probably the result of increased metabolism coincident with the muscular spasms. The unconsciousness that accompanies the convulsion, as well as the mental confusion that follows, I believe to be due to a disturbance in the blood supply of the brain. The work of Florey [41] and Forbes and Wolff [42] indicates that the blood vessels of the brain are under vasomotor control and respond to at least many of the general bodily conditions and drugs which affect the

41. Florey, H.: Microscopical Observations on the Circulation of the Blood in the Cerebral Cortex, Brain **48**:43, 1925.

42. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

blood vessels in other parts of the body. MacRobert and Feinier,[43] Sargent,[44] Kennedy,[45] and Pötzl and Schloffer [46] stated the belief that a disturbance in the cerebral blood supply is an important factor in the epileptic seizure. The last three of these authors have recorded edema of the surface of the brain coincident with the epileptic fit. Additional work is being done to determine, if possible, the meaning of the blood sugar curve found in our experimental animals. It seems likely that the rapid rise in blood sugar with the onset of symptoms is due to a setting free of the available sugar from the liver and other tissues. This is then rapidly burned, causing the blood sugar to fall below normal. This reaction may be concerned, in part if not entirely, with the suprarenal hyperactivity which is indicated in these cases.

It is important to note in the epileptic fit produced experimentally in the dog that the disturbances involving the involuntary muscular system begin first and are followed almost instantaneously by the muscular spasms. Dilatation of the pupils, increased salivation, cardiovascular disturbances, functional disturbance of the digestive canal and bladder and other disturbances in the functions under control of the involuntary nervous system are generally recognized as being associated with the epileptic seizure, but these symptoms have been almost entirely ignored in research on epilepsy. This is perhaps due to the concept that the convulsive spasm involving the voluntary musculature is the direct expression of the disturbance in the cerebral cortex, and that the remaining symptoms are secondary. It is my belief that in the epileptic seizure those symptoms that involve the vegetative and other functions under the control of the involuntary nervous system are more far-reaching and fundamental than the convulsion itself, and that the greatest advance in the future will be made by a careful study of this phase of the epileptic seizure.

Di Renzo [47] noted hyperglycemia during and following epileptic attacks. Lennox [48] reviewed the literature on blood sugar in epilepsy and reported several additional cases that he had studied. He attributed the conflicting views on this subject to his observation that whether or not blood sugar increases with convulsions depends on the amount of

43. MacRobert, R., and Feinier, L.: Epileptic Seizures, J. A. M. A. **76**:500 (Feb. 19) 1921.

44. Sargent, Percy: Some Observations on Epilepsy, Brain **44**:312, 1921.

45. Kennedy, F.: Epilepsy and the Convulsive State, Arch. Neurol. & Psychiat. **9**:567 (May) 1923.

46. Pötzl and Schloffer: The Brain in Epileptic Seizures, abstr., J. Nerv. & Ment. Dis. **64**:303, 1926.

47. Di Renzo, Franco: Researches on Glycemia, abstr., Arch. Neurol. & Psychiat. **15**:649 (May) 1926.

48. Lennox, W. G.: Studies of Metabolism in Epilepsy: II. The Sugar Content of the Blood, Arch. Neurol. & Psychiat. **18**:383 (Sept.) 1927

available dextrose in the body. Isolated convulsions in a well fed person will be attended by a rise in blood sugar, whereas a series of convulsions in a person not recently fed quickly exhausts the glycogen reserves, and the blood sugar becomes lower and lower with each successive seizure. This concept is supported by our experimental data.

Talbot, Hendry and Moriarty,[49] studying eleven cases of epilepsy in children, found the basal metabolism normal or elevated. They quoted Boothby as finding the metabolism normal or elevated in 79 per cent of his twenty-four cases. Bowman and Fry,[50] choosing their cases without reference to age, found the basal metabolism within normal range with a tendency toward low metabolism. These records, it must be noted, were taken in the intervals between seizures and give no indication of the relationship of basal metabolism to the convulsion.

The question arises as to why I get typical epileptic fits in my experimental lesions in the region of the tuber cinereum in the dog while such results have not been obtained by other investigators in this field. The answer probably is to be found in the variety of methods used in producing the lesion. It is interesting to note that in their case histories of twenty-three animals, Bailey and Bremer recorded convulsions in two cases and epileptic attacks in a third. However, these authors attached no significance to these symptoms. There is much reason to believe that the centers in the tuber react readily and more or less specifically to chemical stimuli. Demole[51] found that injecting from 1 to 2 mg. of calcium chloride into the region above and behind the optic chiasm in cats puts the animal to sleep, with the pupils constricted and the heart beat and respiration slowed. On the other hand, injection of potassium chloride has a stimulant effect. These authors placed a sleep center in this region. Spiegel and Saito[52] found that injection of thyroid and ovarian extracts into the lateral ventricle of rabbits had no effect. Pituitary, testis and pineal extracts lowered the blood pressure for twelve minutes, due to vascular dilatation of central origin. Epinephrine, hypertonic salt solution, potassium chloride, sodium sulphate and dextrose solutions increased the blood pressure for thirty minutes. My experimental lesions were made by injecting a

49. Talbot, P. B.; Hendry, M., and Moriarty: The Basal Metabolism of Children with Idiopathic Epilepsy, Am. J. Dis. Child. **28**:419 (Oct.) 1924.

50. Bowman, K. M., and Fry, C. C.: Basal Metabolism in Mental Disease, Arch. Neurol. & Psychiat. **14**:419 (Dec.) 1925.

51. Demole, V.: Pharmakologische Untersuchungen zum Problem des Schlafes, Arch. f. exper. Path. u. Pharmakol. **120**:229, 1927.

52. Spiegel, E. S., and Saito, S.: Beiträge zum Studium des vegetativen Nervensystem: IV. Ueber die harmonale Erregbarkeit vegetativer Zentren, Arb. a.d. neurol. Inst. Wien. Univ. **25**:247, 1924.

weak solution of mercuric chloride (from 0.2 to 1 per cent) or silver nitrate. Lesions have been made in all parts of the diencephalon and basal ganglia, and in some cases the solution was injected into the subarachnoid space and the ventricles. It was only when there was injury to that part of the tuber cinereum containing the nucleus tuberis lateralis, tuberomammillaris and substantia grisea that the convulsions occurred.

I have presented experimental evidence which indicates that the nuclei of the tuber region (nucleus tuberis lateralis, tuberomammillaris, and substantia grisea) may be secretory centers for the suprarenal, thyroid and parathyroid glands. Injection of silver nitrate or mercuric chloride solution in the region of these nuclei in the dog is followed by a series of typical epileptic convulsions. The cases reported in this paper seems to show that these nuclei are pathologic in patients with epilepsy.

The endocrine glands have long been suspected of holding an important relationship to epilepsy. The attempt of many investigators to determine the apparent influence of the suprarenal glands on epilepsy is of especial interest. Fischer,[53] Brüning,[54] Sandor,[55] and Steinthal [56] found that removal of the left suprarenal gland improved and in a few cases entirely cured the patient of epilepsy. On the other hand, Schmieden and Peiper [57] and Küttner and Wollenberg [58] reported negative results following removal of one, and in the latter case one and one half of the suprarenal glands. This operation was performed on the basis of Fischer's idea that removal of the suprarenals reduces muscle tonus and the susceptibility of the patient to convulsions. Brüning believed that the failures which have been reported following this operation may be due to a hypertrophy of the remaining gland tissue. MacKay and MacKay [59] have shown that when one suprarenal gland is removed in the rat the remaining gland increases 68 per cent.

53. Fischer, H.: Extirpation of One Suprarenal for Cure of Epilepsy, abstr., J. Nerv. & Ment. Dis. **61**:317, 1925.

54. Brüning: Removal of Suprarenal Capsules for Epilepsy, abstr., J. Nerv. & Ment. Dis. **55**:133, 1922.

55. Sandor, S.: Extirpation of Suprarenal Gland in Epilepsy, abstr., J. Nerv. & Ment. Dis. **60**:418, 1924.

56. Steinthal: Suprarenal Treatment of Epilepsy, abstr., J. Nerv. & Ment. Dis. **60**:417, 1924.

57. Schmieden and Peiper: Suprarenalectomy in Epilepsy, abstr., J. Nerv. & Ment. Dis. **60**:419, 1924.

58. Küttner and Wollenberg: Suprarenal Operation in Epilepsy, abstr., J. Nerv. & Ment. Dis. **62**:92, 1925.

59. MacKay and MacKay: Compensatory Hypertrophy of the Adrenal Cortex, J. Exper. Med. **43**:395, 1925.

Silverstri [60] was able to bring on epileptic seizures by the injection of suprarenal preparations.

Consideration may now be given to the changes which have been described in the nuclei of the tuber cinereum in the cases reported in this paper, and their significance. The six cases all showed convulsive seizures as the presenting symptom.

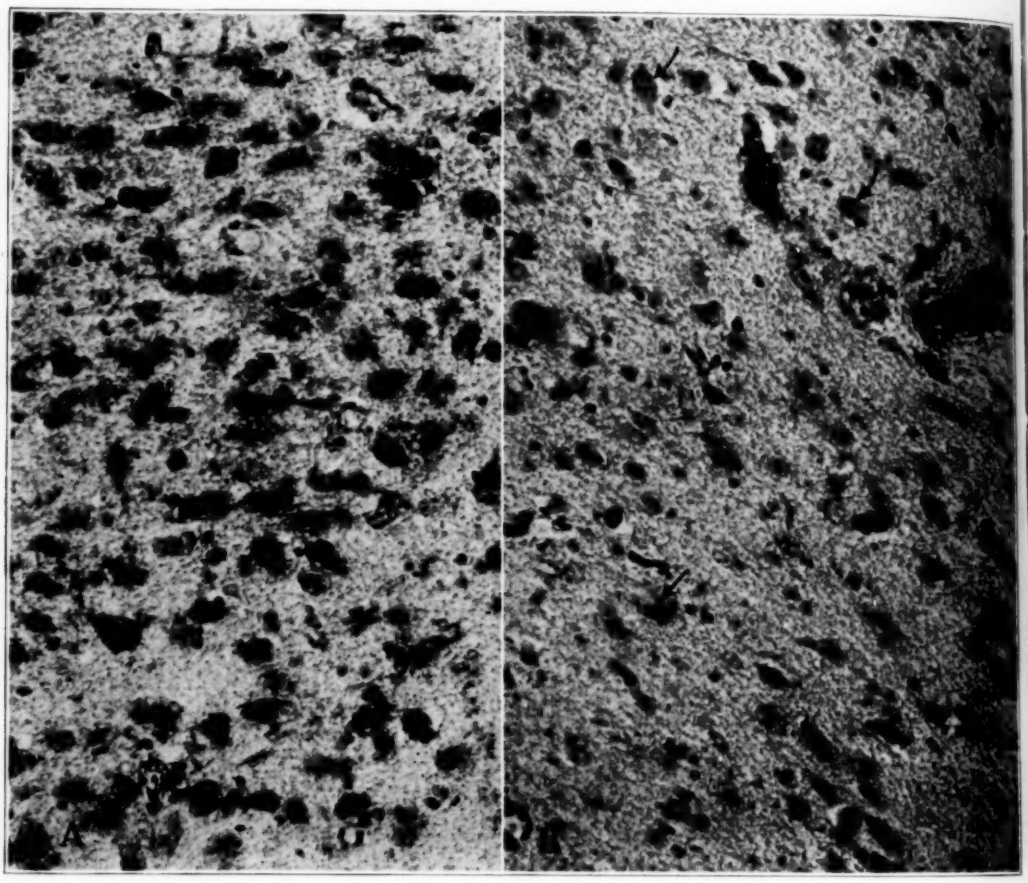

Fig. 10.—Photograph of the substantia grisea to show the cell reduction in epilepsy. *A.* indicates a section from a normal brain (fig. 5); *B.*, section from an epileptic brain (fig. 8). The arrows indicate degenerating cells.

It will be noted that the substantia grisea is the nucleus most affected in all the cases described. It is moreover affected to about

60. Silverstri: Occurrence of Epileptic Seizures After Injection of Adrenalin Preparations, abstr., Endocrinology **3**:349, 1919.

the same degree in all cases. The cells of the substantia grisea of the third ventricle are reduced to from 15 to 35 per cent of the normal number. The cases of epilepsy were apparently in the more advanced stages when mental deterioration was marked. The shrinkage in the area of the substantia grisea, the small increase in glia cells (from 2 to 3 times that of the normal), the frequent hyperemia and the general chromatolysis seem to indicate a slow cell degeneration which had been

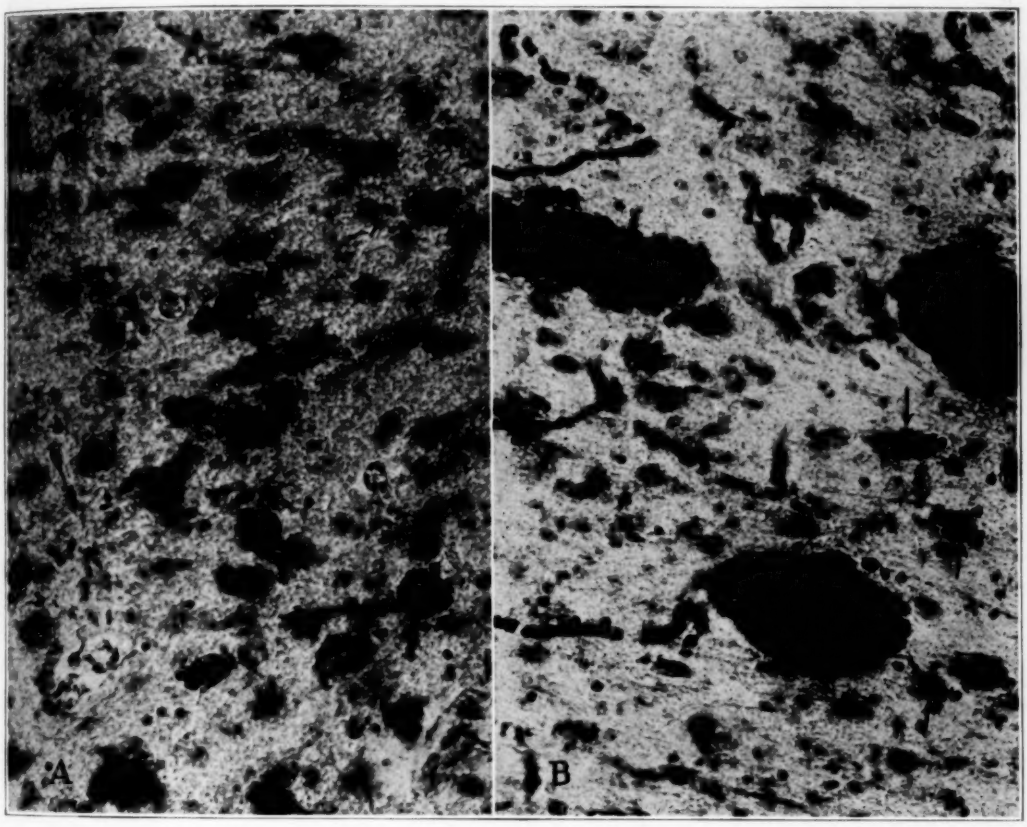

Fig. 11.—Photograph of the nucleus tuberomammillaris. *A*. indicates a normal brain (fig. 5); *B*., an epileptic brain (fig. 8). Note the reduction of cells in *B*. The arrows indicate degenerating cells.

going on for a long time and was still in progress at the time of death. The nuclei of the two sides of the brain were usually affected to about the same degree. Usually, the basilar portion of the nucleus and the zone of cells immediately adjoining the third ventricle were affected most, frequently suffering almost complete destruction. This

general pattern to which the cell degeneration conforms suggests that the agent responsible for this destruction may be closely related to the blood supply of this region; either being carried in the blood stream or consisting of an interference with the blood supply.

Next to the substantia grisea, the nucleus tuberis lateralis was most affected in the cases studied. There was a loss of 60 per cent of the

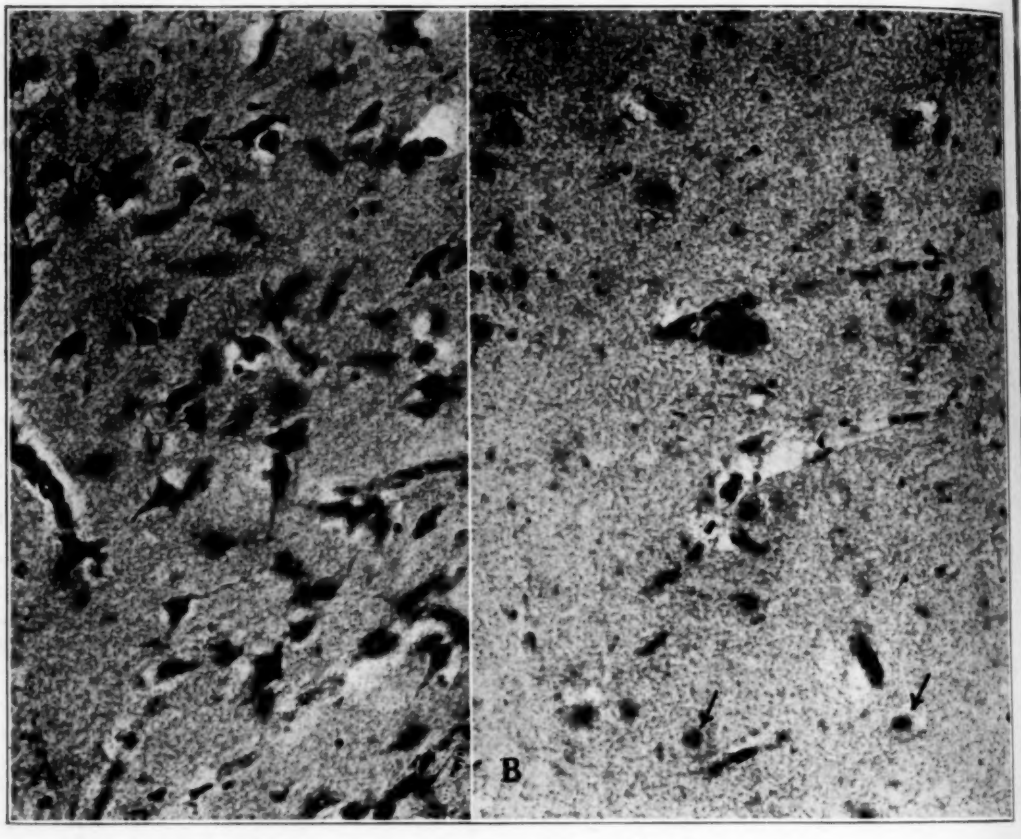

Fig. 12.—Nucleus tuberis lateralis. *A.* indicates a normal brain; *B.*, an epileptic brain. The arrows indicate degenerating cells.

cells in case 1; 75 per cent in case 2; 80 per cent in case 3; 55 per cent in case 4; 70 per cent in case 5, and 65 per cent in case 6. There was very marked and widespread chromatolysis in the nucleus tuberis lateralis in all these cases. Furthermore, shrinkage, proliferation of glia and other general indications point to degenerative processes which are of long standing and yet were active at the time of death.

The nucleus tuberomammillaris is less affected than the two nuclei already discussed. There is cell loss in all cases. In case 1 there is only a loss of about 15 per cent of the cells. In the others the cell loss ranges from 35 to 55 per cent. There is from 60 to 85 per cent chromatolysis in all remaining cells. This chromatolysis is distributed through all stages. Here, again, the general features are suggestive of a slow degeneration of long standing.

Although a varying amount of chromatolysis sometimes occurs in the basal optic ganglion and the paraventricular nucleus, this does not seem to appear in sufficient amounts or with enough regularity to justify connecting these nuclei with epilepsy.

The present state of knowledge does not justify a statement that lesions in the nuclei of the tuber cinereum are responsible for epilepsy, but combining our experimental data with the pathology which has been described in the cases here reported, there seems to be evidence that this region of the brain may play an important part in causing repeated epileptiform seizures. One seems to be justified in considering the nuclei of the tuber as secretory centers controlling certain of the glands of internal secretion. It is impossible to say as yet which nucleus controls which gland. The suprarenal glands seem certainly to have a secretory center in the region of the tuber cinereum. There is slight evidence, by no means conclusive, to indicate that the substantia grisea may be the particular cell group which is concerned with the suprarenal gland.

If one is to conceive of the substantia grisea, nucleus tuberis lateralis and nucleus tuberomammillaris as secretory centers of the suprarenal, thyroid and parathyroid glands, the question arises as to how far and in what manner they may be concerned in producing the symptoms characteristic of epilepsy. The experimental evidence seems to show clearly that the epileptic seizure is characterized by a hypersecretion of the suprarenal and either the thyroid or parathyroid, or both, rather than a diminished function of these glands. As secretory centers of the glands of internal secretion the nuclei of the tuber would form part of a very important mechanism for regulating the function of these glands. From the nature of this function one might suppose that this regulation is dependent on the contents of the blood stream, much as the respiratory centers in the medulla are influenced by the carbon dioxide content of the blood. If this is the case, the cells in the tuber cinereum are so constructed as to react to certain specific chemical substances carried by the blood stream. The very nature of these cells, therefore, would make them more susceptible to other chemical or toxic substances than would be other cells of the brain which are designed primarily to react to stimuli conducted over nervous pathways. Further-

more, the cells of the three nuclei of the tuber might react differently to any one chemical substance. This consideration may explain why one sometimes observes a selective degeneration in one or more of these nuclei without affecting other parts of the brain. Furthermore, it may be possible for these nuclei to react differently to different toxins or other agents, thereby producing different symptoms in different cases.

Considering the nuclei of the tuber cinereum as secretory centers for the thyroid, parathyroid and suprarenal glands, can one perhaps explain idiopathic epilepsy on the basis of a functional disturbance of the cells in this region? If so, what must be the nature of that disturbance? The symptoms affecting the involuntary functions of the body might be explained as being due to a hypersecretion of the suprarenal glands. The spasms involving the voluntary musculature are not so easy to explain. That they are concerned with either the thyroid or parathyroid, or both, is indicated in the experiments on dogs. I have shown that the muscular spasms experimentally produced cease immediately with the ligation of one, or sometimes both, thyroid and parathyroid glands. Little is yet known of what effect a hypersecretion of the parathyroids would have on the body. The convulsions in the experimental animals appear too soon after the operation to be considered as parathyroid tetany; furthermore, they present very little similarity to typical parathyroid tetany. A study of the blood chemistry in the experimental animals showed no significant rise in blood calcium as might be expected were the parathyroid hyperactive. Much more additional work needs to be done on the relationship of the thyroid and parathyroid to the tuber cinereum of the brain and of the part which this mechanism plays in epilepsy or other diseases. It seems probable, however, that the thyroid-parathyroid complex is under the influence of the tuber, and that this mechanism plays a rôle in the etiology of epilepsy.

SUMMARY

The present report is concerned chiefly with a study of the nuclei of the tuber cinereum region in six human brains. These are from six cases of epilepsy. There was marked shrinkage and frequently hyperemia in the wall of the third ventricle and at the base of the tuber cinereum. The cells of the substantia grisea were reduced to from 15 to 35 per cent of the normal number. Chromatolysis was general among the remainder of the cells, and the glia cells were increased to two or three times the normal number. Neuronophagia was common. There was a loss of from 35 to 80 per cent of the cells in the nucleus tuberis lateralis, with marked and widespread chromatolysis among the remaining cells. Shrinkage, proliferation of glia and neuronophagia

were common in this nucleus. The cell loss in the nucleus tuberomammillaris varied from 15 in one case to from 35 to 55 per cent in the remaining cases. From 60 to 85 per cent of the remaining cells in this nucleus showed chromatolysis. Neuronophagia was common.

These observations may indicate that the degeneration in the substantia grisea of the third ventricle is concerned with the mental deterioration of epilepsy. The nucleus tuberis lateralis, nucleus tuberomammillaris and perhaps also the substantia grisea may be concerned with the other symptoms which are characteristic of epilepsy.

The three nuclei of the tuber are apparently secretory centers for the thyroid, parathyroid and suprarenal glands. Perhaps the epileptic seizure can be explained as an abnormal, uncontrolled discharge of impulses from these centers.

DEFICIENCY OF CATALYTIC IRON IN THE BRAIN IN SCHIZOPHRENIA*

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The histologic approach to schizophrenia has failed. This was brought out forcibly in 1925 by Dunlap,[1] who concluded that the changes described in the literature were not characteristic, and that identical changes might be found in the brains of mentally normal persons killed by accident. The past four years have brought forward nothing of consequence to enlighten the situation, although contributions have been numerous and at least one synthetic review has been offered.[2]

This does not mean that there is no histologic alteration in the brain of the schizophrenic person. It indicates merely that, with the methods so far applied and the controls so far run, significant changes have not been detected. It is a criticism rather of our methods than of our eyes. By the application of already known methods to the chemistry of the cell, however, there is opened a different approach that may lead to a better understanding of the disease.

While histologists have attempted unsuccessfully to solve the problem, chemists have disclosed a possible solution to one of the many problems of schizophrenia. The history of this search dates back twenty years to the ideas of Mott[3] regarding oxidative processes in the cells, but the graphic demonstration was brought to the fore only during the past year, when, by administering a mixture of carbon dioxide and oxygen, Loevenhart, Lorenz and Waters[4] were able to bring about startling changes in the behavior of catatonic patients. From being stuporous, mute and resistive, these patients became active and communicative. I have repeated these experiments and in certain instances have obtained similar results. I am not entirely satisfied, however, with the explanation of these workers concerning the mech-

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* From St. Elizabeth's Hospital.

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1. Dunlap, C. B.: The Pathology of the Brain in Schizophrenia, Schizophrenia vol. of the Assn. for Res. in Nerv. & Ment. Dis., New York, Paul B. Hoeber, Inc., 1927.

2. Buscaino, V. M.: Ricerche istoneuropatologische e del liquor in dementi precoci. Quarta rivista sintetico-critica, Riv. di patol. nerv. **34**:181, 1929.

3. Mott, F., quoted by Golla, F. L.: Some Recent Work on the Pathology of Schizophrenia, Proc. Roy. Soc. Med. **22**:31, 1929.

4. Loevenhart, A. S.; Lorenz, W. F., and Waters, R. M.: Cerebral Stimulation, J. A. M. A. **92**:880 (March 16) 1929.

anisms involved. They likened the effects of carbon dioxide to those of sodium cyanide in producing increased cerebral activity through decreased oxygen fixation. This is contrary to the experience of aviators and others, whose mental activities diminish as oxygen tension falls. Divers and "sand hogs," however, who work under high pressure, are familiar with the stimulating, even exhilarating, effects of increased oxygen tension. My colleagues and I have experienced both effects through the kindness of the Deep Diving Experimental Unit at the U. S. Navy Yard in Washington.

In the experiments undertaken by Loevenhart, as well as in our own, the mixtures of gas administered contain a much higher percentage of oxygen than ordinary air. I would suggest, therefore, that the high concentration of oxygen may have much to do with the renewed activity of the mental processes, and that the carbon dioxide, by increasing respiration, brings about a more rapid saturation of the tissues with oxygen. In other words, the cerebral cells in these schizophrenic patients may be unable to function normally because they cannot utilize the oxygen that is brought to them under existing conditions of atmospheric pressure, although they may perform their normal functions when the tension of oxygen is increased sufficiently to compensate for the defect.

A number of factors may operate to reduce the amount of oxygen utilized, such as slowed circulation, reduced intake of oxygen, etc. The basis of the present work, however, is the hypothesis that the cells of the cerebral cortex are unable to function normally under adequate oxygen intake because they are deficient in substances essential for oxidation-reduction processes.

Among the substances involved in cellular oxidation, two are of outstanding importance, sulphydryl compounds and iron.[5] Neutral sulphur was investigated twenty years ago by Koch and Mann[6] who concluded: "It does not seem then unreasonable to suppose that the subjects of the mental disorder (dementia praecox) may possibly possess a general bodily inherent deficiency for oxidation processes." Further investigation of the rôle of sulphur, and especially of glutathione, has been undertaken by Dr. Anne Yates in the laboratory of St. Elizabeth's Hospital.

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5. I recognize the possible significance of copper, but am unable to evaluate it for lack of data. The catalytic activity of this element in oxidation-reduction in vitro seems even greater than that of iron (Warburg, O.: Biochem. Ztschr. **187**:255, 1927), and the importance of copper as a hematogenic agent has recently been recognized. The histochemical reaction seems to be identical, in the Macallum process, with that of iron.

6. Koch, W., and Mann, S.: A Chemical Study of the Brain in Healthy and Diseased Conditions, with Especial Reference to Dementia Praecox, Arch. Neurol. & Psychiat. (England) **4**:174, 1909.

The importance of iron as a catalytic agent in oxidation-reduction processes has repeatedly been emphasized. Traces of iron are practically necessary for the utilization of oxygen by glutathione and other sulphydryl radicals. Iron is a constituent of almost every living cell (copper being an occasional substitute). Cyanide is lethal to cells through suppression of oxygen metabolism, an effect that may be brought about by combination of the cyanide with the iron of the cell to form an inert readily diffusible ferrocyanide. At all events, the injection of sodium cyanide into the carotid artery of a rabbit diminishes the quantity of iron demonstrable subsequently in the corresponding hemisphere of the brain (fig. 1). Iron is most prominent in the Nissl granules and in the chromatin of the nucleus and nucleolus, the probable location of the major metabolism. Nearly forty years ago, Macallum [7] with a burst of prophetic insight declared that the fundamental life substance was an iron compound, and that life itself was to be referred to the constant oxidation and reduction of this compound.

IRON IN THE BRAIN

Iron was the second element to be discovered in the brain, Spielman,[8] in 1766, finding that a magnet attracted particles from the ash. Nearly a century later appeared the only quantitative study, Breed [9] giving the ratio of 1.23 parts of ferric pyrophosphate to 100 parts of ash.

This equals about 18 mg. of iron per hundred grams of dried brain. Breed's observations are scarcely comparable with mine since no information is given concerning the material utilized or the method applied.

Iron has recently aroused much interest among neuropathologists, but Spatz,[10] no matter how significant his work may be with regard to the iron in microglia cells in dementia paralytica, went far afield in explaining how it came there. To account for its presence by assuming a greater permeability of the cerebral capillaries is to neglect the work of Macallum, Mann [11] and, more recently, Muhlmann,[12] who recog-

7. Macallum, A. B.: Studies on the Blood of Amphibia, Tr. Canad. Inst. **2**:45, 1890-1891.

8. Spielman, quoted by Thudichum, J. L. W.: Die chemische Konstitution des Gehirns des Menschen und der Tiere, Tübingen, 1901.

9. Breed: Analyse der Asche des menschlichen Gehirns, Ann. de chem. **80**: 124, 1851.

10. Spatz, H.: Zur Eisenfrage, besonders bei der progressiven Paralyse, Zentralbl. f. d. ges. Neurol. u. Psychiat. **27**:171, 1921; Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:138, 1924, for partial revision of this opinion.

11. Mann, G.: Physiological Histology, London, Oxford University Press, 1902.

12. Muhlmann, M.: Hämatoxylin als Reagens auf Eisen, Virchows Arch. f. path. Anat. **266**:697, 1928.

nized the importance of iron in the parenchymatous cells. Regarded from this point of view, the iron observed by Spatz in the microglia cells is waste iron, released by the disintegration of the ganglion cells in the cerebral cortex, and it is therefore a good index of the activity of the destruction.

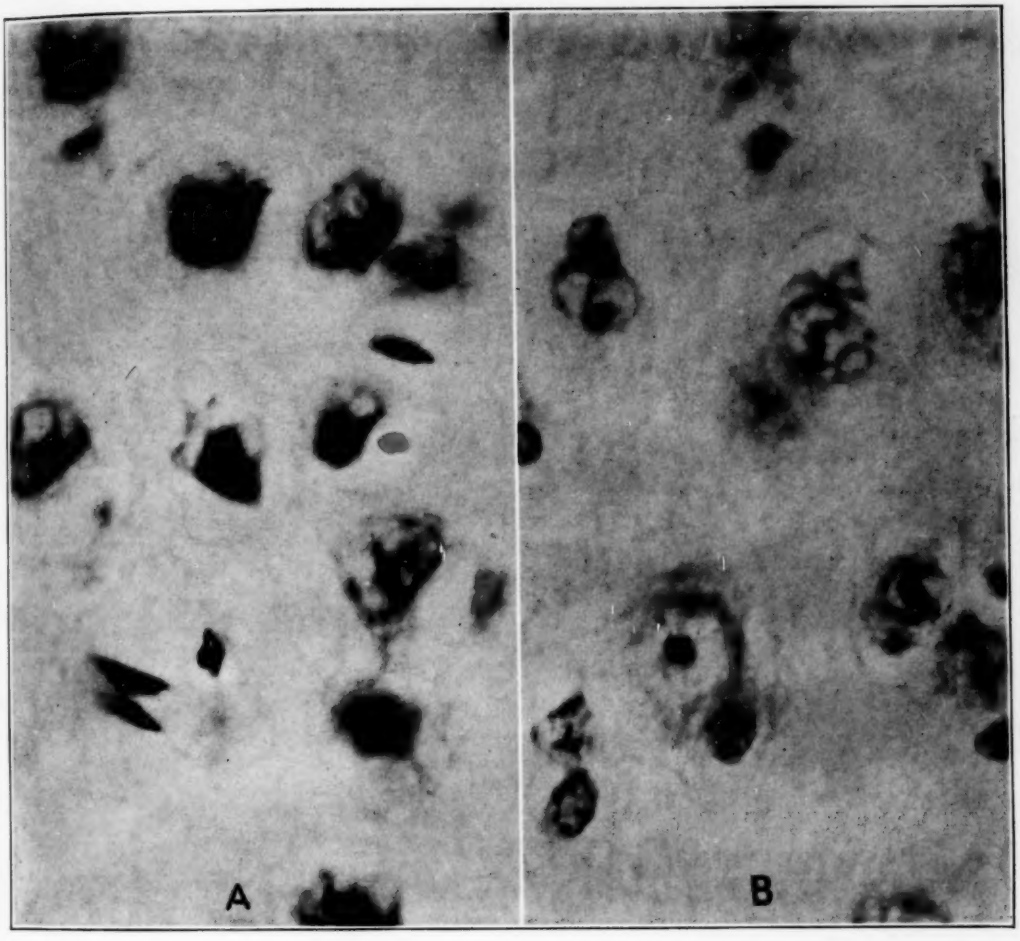

Fig. 1.—Cerebral cortex from left (*A*) and right (*B*) hemispheres of a rabbit (Ac. 264) after the injection of 1 per cent sodium cyanide solution into the right carotid artery. Macallum hematoxylin method for iron.

Nicholson [13] has published some interesting work on the distribution of catalytic iron in the ganglion cells. First using the Nissl technic,

13. Nicholson, F. M.: The Changes in Amount and Distribution of Iron-Containing Proteins of Nerve Cells Following Injury to Their Axones, J. Comp. Neurol. **36**:37, 1924.

then decolorizing and staining for iron, he demonstrated that the Nissl granules contain iron and that this iron is diffused following section of the axon. The main difference between the pictures obtained by the two methods is the relatively richer detail of the nuclear structure in the hematoxylin preparation.

The cellular iron is in organic combination and must first be released, following which a variety of methods can be used for its demonstration. The prussian blue reaction is sensitive, but far superior, on account of its delicacy, is the Macallum hematoxylin method. This depends, as Jones [14] has indicated, on the fact that the iron in the cell acts as a mordant and combines with the hematoxylin to form an insoluble bluish-black lake. Difficulties in the utilization of this method have been pointed out by Macallum [15] and others. Fixation of the tissue in a watery solution permits rather rapid diffusion of iron, so that results are unreliable on old material. A better procedure is fixation in strong alcohol. Only after a number of months in alcohol does the intensity of the reaction fade. The minutest trace of acid or alkali will interfere with the reaction, and neutral salts are apt to prevent satisfactory staining. For this reason the method is much better adapted to showing iron in the nucleus, where salts are practically absent, than that which is deposited about vessels or contained in the microglia. Dead cells take up iron, the basis of the Heidenhain method of staining, and histologic results on material obtained a number of days after death are unsatisfactory.

My own researches may be considered under two headings: histochemical and quantitative.

HISTOCHEMICAL STUDIES

Blocks from the right frontal pole, taken at the time of necropsy, were fixed in 95 per cent alcohol, for from two to seven days, and then embedded in paraffin. Sections were cut at 10 microns and processed by the prussian blue reaction and by the modification of Macallum's method described by Anderson.[16] On each slide were mounted two sections, so that technically comparable results might be obtained. An effort was made to have the cortex of the two sections almost in apposition, so that under the microscope a rapid back-and-forth comparison could be made. Photomicrographs were taken of each section on the two halves of the same photographic plate, everything except the field being maintained constant. Similar layers, even similar cells, were compared.

Preliminary controls were run. Sections from near the surface of the block showed no difference from those at a deeper level. Sections fixed for two days showed no difference (in the same brain) from those fixed for two weeks before

14. Jones, H. W.: The Distribution of Inorganic Iron in Plant and Animal Tissues, Biochem. J. **14**:654, 1920.

15. Macallum, A. B.: Die Methoden und Ergebnisse der Mikrochemie in der biologische Forschung, Ergebn. d. Physiol. **7**:552, 1908.

16. Anderson, J.: How to Stain the Nervous System, Edinburgh, E. & S. Livingstone, 1929.

embedding. Sections on the upper part of the slide were identical with those on the lower end. Further controls were established. Patients of the same psychiatric reaction type were chosen for this purpose and two sections from different persons were mounted on the slide for comparison. Sex and age made no appreciable difference, other factors being constant. The height of the fever before death produced changes in the cytoplasm but none in the nucleus. The time between death and necropsy had a definite and uncontrollable effect, the nucleus becoming heavier and poorly differentiated. It was therefore determined to exclude cases examined more than twenty-four hours post mortem. A lingering illness as opposed to a sudden death made no difference.

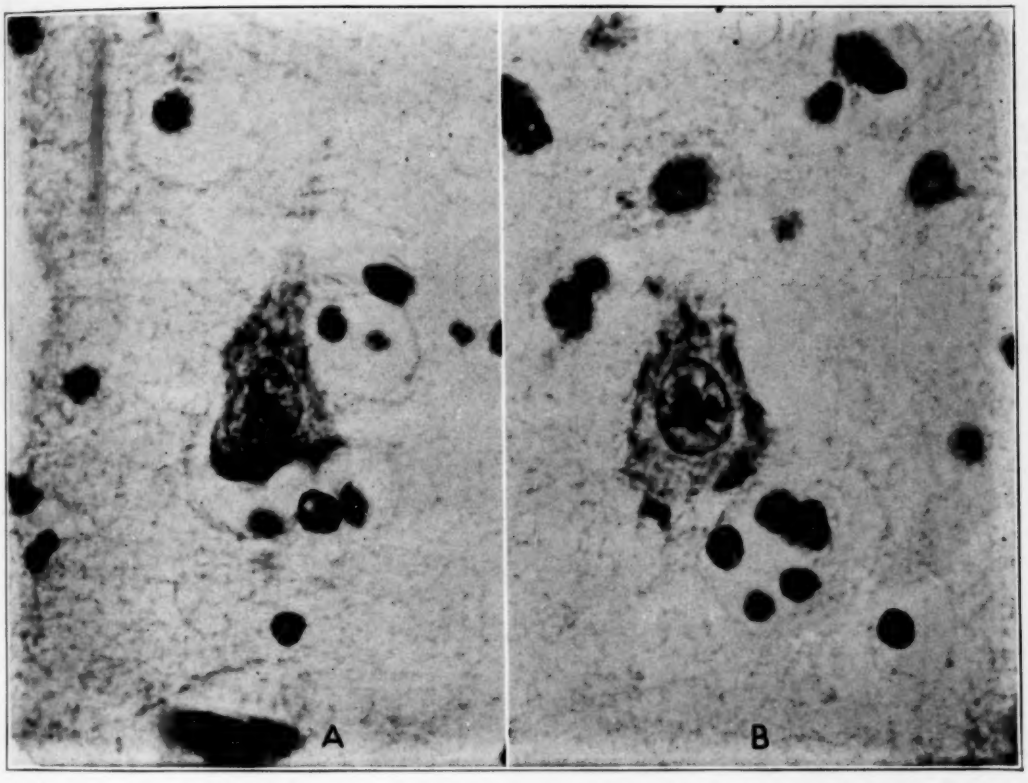

Fig. 2.—Cerebral cortex of frontal pole, treated as described in the text. *A* shows the schizophrenic (53.51) and *B* the paranoid (5376) state. Large pyramidal cells are shown.

I was unable to obtain material from mentally normal persons. A comparison would have been valuable. I do not consider it of paramount importance in my work since I have chosen material for differentiation from different types of persons, in the final analysis comparing the schizophrenic person with the paranoid, the epileptic, the manic-depressive—what might be termed "pure culture differentiation."

When a Macallum preparation is examined under a high power, a sharply cut nuclear picture is observed, with some indication of cytoplasmic structure. The outlines of the cells are pale blue with darker chromatin masses showing the characteristic distribution. These cytoplasmic structures are so labile, however, that little importance is

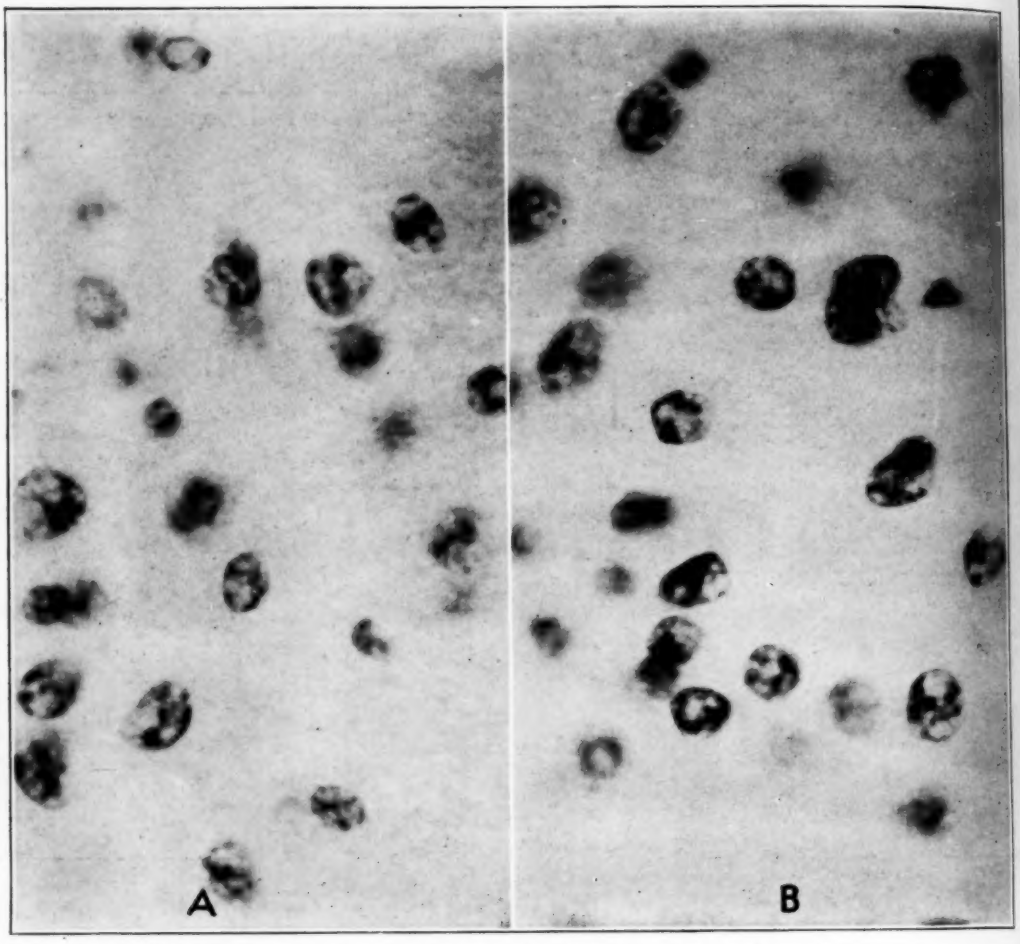

Fig. 3.—Same specimen as in figure 2. Small pyramidal cells are shown. *A* shows the schizophrenic (5351) and *B* the paranoid (5376) state.

accorded them. Moreover, the Nissl granules have been subjected to limitless study without tangible results in schizophrenia. My attention, therefore, has been focused on the nucleus. The nuclear membrane is more or less sharply outlined, and, contrary to the prevailing observation in thionine stains, the chromatin network is sharply distinguishable, the nucleolus staining intensely black. If the prussian

blue reaction is chosen and the preparation examined with a red filter, an identical though somewhat paler picture is observed.

It is not possible in every case to determine by inspection which cortex stains more heavily. There are differences in different parts of the same lamina, in different laminae, even in different cells almost in juxtaposition, but the schizophrenic can be distinguished from the paranoid in more than 70 per cent of the cases by this specific reaction

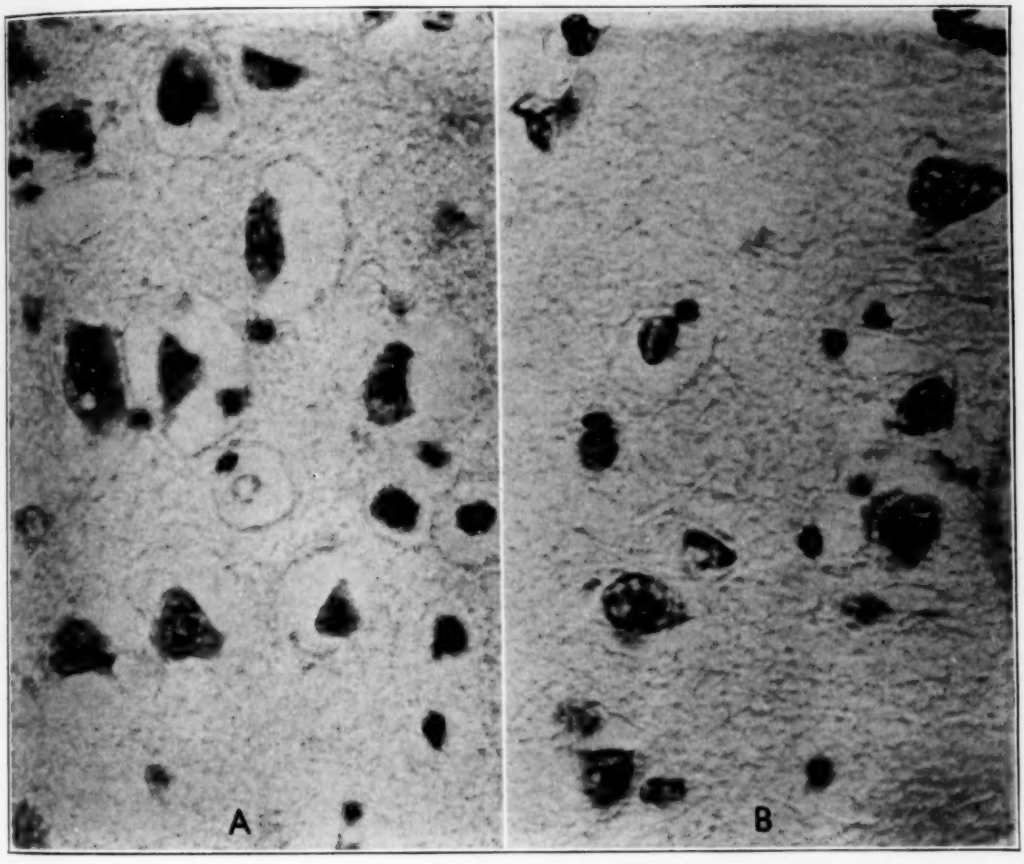

Fig. 4.—Same conditions as in figure 2. Polymorphous cells are shown. *A* shows the schizophrenic (5449) and *B* the paranoid (5427) state.

for iron. In the cortex from a typical case of schizophrenia (figs. 2, 3 and 4) the nuclear membrane of the ganglion cell is thin, sometimes almost to the point of extinction;[17] the chromatin masses are delicate, and the nucleolus is smaller and paler than in a typical case of a paranoid state. Some cells, particularly those in the infragranular strata,

17. If the metabolic activity is most pronounced at the nuclear membrane, as seems probable, this is a suggestive observation. See figure 2.

have an almost shadowy nucleus. In some instances the various cortical laminae show decided differences in the iron reaction, a factor that may, on further study, show significant variation with the type of behavior present, hebephrenic or catatonic, but the material is too small as yet to be conclusive. No difference is noted in the nuclei of the neuroglia cells in different sections.

QUANTITATIVE CHEMICAL STUDIES

My colleagues at the U. S. Naval Medical School in Washington, and especially their chemist, Mr. Reese, carried out the painstaking and intricate analyses of tissues which complement this investigation. As I have already indicated, the only quantitative analysis of human brain with which I am acquainted is that contained in a brief note in Liebig's *Annalen* for 1851. Some brains from animals have recently been examined in a study of iron in foodstuffs.[18] There are consequently no established normals, and one has again had to rely on "pure culture differentiation" with regard to the types of psychoses.

At the time of necropsy the right frontal lobe is amputated, and, after removal of the membranes and blood vessels, the cortex is washed and then resected. After mincing and weighing, the material is dried to constant weight, then ground and submitted to analysis. The method used[19] for the estimation of iron had to be modified to some extent. It was found that 1 Gm. of tissue did not oxidize completely, so 250 mg. of the dried brain was used in the estimation. The standard was made up with 0.0125 mg. of iron per cubic centimeter.

The results are given in table 1. From this table it may be seen that the average iron content is slightly lower in the schizoid than in the paranoid or cycloid group, the epileptoid group being too small for consideration. Giving due weight to the probable errors involved, however, the difference is undoubtedly significant, since it is four times its probable error. This figure indicates that there is less than 1 chance in 100 of having samples of similar size obliterate the difference.

There is no evident variation with sex or race, age or weight of brain, but there is a rather high rate in dementia paralytica. This is to be expected from the abnormal number of mesodermal elements found in the cortex in dementia paralytica as well as from the atrophy and condensation of the cortex. In any case it must be reiterated that such quantitative estimations are not completely reliable as indexes of the catalytic iron present in the ganglion cells, on account of the rather large number of glia cells also present in the cerebral cortex. The

18. Elvehjem, C. A., and Peterson, W. H.: Iron Content of Animal Tissues, J. Biol. Chem. **74**:433, 1927.

19. Fowweather, F. S.: Determination of Iron in Tissues, Biochem. J. **20**:93, 1926.

TABLE 1.—*Quantitative Analysis of Cerebral Cortex for Iron*

Aut.	Age	Sex	Race	Mental Diagnosis	Physical Disease	Brain Weight	Iron in Mg. per 100 Gm. Dried Cortex
				Schizoid Group			
5444	37	M	W	Hebephrenic dementia praecox	Tuberculosis of lungs	1,268	44.1
5425	47	M	W	Catatonic dementia praecox	Tuberculosis of lungs	1,432	46.8
5449	37	F	C	Hebephrenic dementia praecox	Carcinoma of uterus	1,170	44.1
5276	27	F	C	Catatonic dementia praecox	Tuberculosis of lungs	1,180	42.6
5447	55	F	C	Catatonic dementia praecox	Tuberculosis of lungs	1,078	44.1
5460	53	F	W	Hebephrenic dementia praecox	Strangulated hernia	1,200	44.1
5464	30	F	W	Hebephrenic dementia praecox	Tuberculosis of lungs	1,123	46.9
5471	63	M	W	Hebephrenic dementia praecox	Bronchiectasis	1,515	44.1
5422	39	F	W	Dementia paralytica	Tuberculosis of lungs	1,078	46.8
5446	55	M	C	Dementia paralytica	Dementia paralytica	1,350	50.0
5468	42	F	C	Dementia paralytica	Bronchopneumonia	1,019	46.9
5433	61	F	C	Psychosis with cerebral arteriosclerosis	Myocarditis	1,195	50.0
5442	67	F	W	Undifferentiated psychosis	Arteriosclerosis	1,195	44.1
5456	80	F	W	Senile dementia	Arteriosclerosis	1,010	44.1
				Average for schizoid group			45.62 ± 0.41 mg.
				Paranoid Group			
5423	50	M	W	Paranoid dementia praecox	Carcinoma of intestine	1,360	48.5
5426	60	M	C	Paranoid dementia praecox	Carcinoma of lung	1,173	42.6
5429	48	M	W	Paranoid dementia praecox	Chronic nephritis	1,475	46.9
5430	63	M	W	Paranoid dementia praecox	Carcinoma of stomach	1,450	53.6
5437	62	F	C	Paranoid dementia praecox	Chronic nephritis	1,063	46.9
5458	47	M	W	Paranoid dementia praecox	Tuberculosis of lungs	1,550	46.0
5472	51	M	W	Paranoid dementia praecox	Tuberculosis of lungs	1,402	50.0
5264	86	F	W	Senile dementia	Bronchopneumonia	1,150	46.8
5421	83	F	W	Senile psychosis	Bronchopneumonia	1,002	46.8
5451	79	M	W	Senile psychosis	Carcinoma of stomach	1,310	46.9
5465	76	F	W	Senile psychosis	Cerebral thrombosis	1,163	46.9
5467	70	F	W	Senile psychosis	Arteriosclerosis	992	50.0
5266	40	M	C	Dementia paralytica	Dementia paralytica	1,309	51.9
5427	64	F	C	Psychosis with cerebral arteriosclerosis	Arteriosclerosis	1,040	53.6
5438	57	F	C	Psychosis with cerebral arteriosclerosis	Myocarditis	1,104	44.1
5439	65	M	C	Psychosis with cerebral arteriosclerosis	Myocarditis	1,201	46.9
5452	57	M	W	Psychosis with cerebral arteriosclerosis	Ulcerative colitis	1,365	44.1
5459	79	F	C	Senile psychosis	Endocarditis	970	53.6
5450	56	F	W	Psychosis with somatic disease	Cardiorenal disease	1,240	46.9
5435	55	M	W	Undifferentiated psychosis	Fractured femur	1,336	46.9
5453	84	M	W	Undifferentiated psychosis	Tuberculosis of kidney	1,210	50.0
				Average for paranoid group			49.08 ± 0.45 mg.
				Cycloid Group			
5434	41	M	W	Involutional melancholia	Suicide	1,460	50.0
5445	51	M	W	Agitated depression	Coronary thrombosis	1,356	46.9
5469	56	F	C	Manic-depressive psychosis	Septic arthritis	1,265	46.9
5424	72	M	C	Dementia paralytica	Pyelonephritis	1,257	46.8
5432	64	M	W	Dementia paralytica	Bronchopneumonia	1,125	53.6
5455	44	F	W	Dementia paralytica	Acute malaria	1,110	46.9
5457	67	M	W	Dementia paralytica	Acute malaria	1,275	50.0
5440	65	M	C	Psychosis with cerebral arteriosclerosis	Prostatic abscess	1,262	44.1
4548	61	F	W	Psychosis with cerebral arteriosclerosis	Acute enteritis	1,052	44.1
				Average for cycloid group			47.70
				Epileptoid Group			
5279	29	M	W	Epileptic psychosis	Status epilepticus	1,390	46.8
5443	43	M	W	Epileptic psychosis	Coronary thrombosis	1,662	44.1
5463	21	M	C	Epileptic psychosis	Tuberculosis	1,123	50.0
				Average for epileptoid group			46.97
				Undifferentiated Group			
5429	86	M	C	Senile psychosis	Arteriosclerosis	1,066	44.7
5431	54	M	W	Imbecility	Convulsion	1,345	50.0
5470	16	F	W	Juvenile dementia paralytica	Dysentery	540	46.9
Ac.248	64	F	W	No psychosis	Pernicious anemia	1,160	42.6

Note: The iron content of dried blood is given as 47.5 mg. per hundred grams.

nuclei of these glia cells evidently contain an abundance of iron. Therefore, I consider even small differences in the quantitative figures to be of importance, since the presence of the glia cells would tend to mask the macrochemical differences between different cases.

TABLE 2.—*Variations in Iron Content According to Sex and Race*

Class	Cases	Average Iron
White male	19	48.0
Colored male	9	47.5
White female	13	47.0
Colored female	10	47.2

TABLE 3.—*Variation in Iron Content in Certain Diseases*

Class	Cases	Average Iron
Neurosyphilis	8	48.3
Tuberculosis	10	47.1
Carcinoma	5	47.1
Cardiac and renal	12	47.3

SUMMARY

Quantitatively and histochemically, there has been found a deficiency of iron in the cortical ganglion cells in schizophrenia. The lack of this catalytic agent, so essential for the utilization of oxygen by these cells, may underlie certain features in the symptomatology of the psychosis.

MULTIPLE GLIOMAS OF THE BRAIN *

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ALBANY, N. Y.

Gliomas of the brain are common enough but since the works of Achucarro, Ramón y Cajal and del Rio Hortega, of Spain, and of Percival Bailey, Harvey Cushing, Wilder Penfield and J. H. Globus, in this country, much histologic interest has been aroused in these tumors. Bailey and Cushing [1] and Bailey [2] have made detailed clinico-pathologic studies of the tumors of the glioma group. In contrast to solitary gliomas, multiple gliomas have been observed but rarely. Because of this, the case of multiple gliomas of the brain presented is of interest.

REPORT OF CASE

Clinical History.—M. A., a cattle dealer, aged 44, was admitted, in 1928, to the service of Dr. George S. Amsden, Albany Hospital, as suffering from mental disease. His wife, a son and two cousins gave the information that the patient had been in an automobile accident a little over four weeks before. He was struck on the head but did not lose consciousness. About two days later, his family noticed that his speech was altered. He could not pronounce words well. He also became unsteady on his feet. About four days after the accident, he complained of severe headache and dizzy spells. His speech became gradually less distinct, and for the last two weeks he had not been able to talk. He gradually became more unsteady on his feet, and five days before admission he fell while walking; since then he had been confined to bed. There was a partial paralysis on the right side, which gradually became worse. During the last five days, he had been entirely incontinent. He also had frequent vomiting spells, especially on sitting up. He was untidy, expectorating on the bed clothing. Emotionally, he was unstable and cried considerably.

A cousin gave the information that for a few months before the accident the patient had been worrying considerably and was irritable at times, especially at home. He had expressed the idea that his head felt queer, and that he was afraid he would lose his mind.

He was said never to have had a day's sickness previous to the onset of the present illness. Longevity and mental clearness were family characteristics. His father died at the age of 78 from an unknown cause. Three brothers and one sister were living and well.

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* Submitted for publication, Feb. 20, 1930.

* From the Department of Pathology, Albany Medical College, and the Pathological Laboratory of the Albany Hospital.

1. Bailey, P., and Cushing, H.: A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis, Philadelphia, J. B. Lippincott Company, 1926, p. 175.

2. Bailey, P.: Histologic Atlas of Gliomas, Arch. Path. **4**:871 (Dec.) 1927.

Physical Examination.—The patient followed the activities of visitors with inquiring eyes and by rotating his head, but he apparently did not sense the meaning of their movements as he should. He would raise his arm to permit the band of a blood pressure apparatus to be placed about it, but would not answer a command to do so. When asked to protrude his tongue, a delay of several seconds was noticeable before he started the movement, and then it was often necessary to demonstrate the procedure to him. Crying spells were frequent. When asked a question he generally smiled before he attempted to answer it. As a rule, his attempts to speak were either only movements of the lips or a meaningless jumble. On one occasion he said "better" when asked about his condition.

The skull was symmetrical, there being no exostoses or depressions. There were no tender points and no physical evidences of fracture. The ears were symmetrical, with no tender points about the mastoids. The pupils were equal (2 or 3 mm.) and regular and reacted to light directly and consensually. Extra-ocular movements were not obtainable. There was no evidence of drooping of the lids. Examination of the eyegrounds showed a slight congestion of the retinal veins; the physiologic cup of the optic disks appeared obliterated. The teeth were in a fair condition. The tongue was thick and did not protrude well, but appeared to deviate to the right. The mucous membranes were of good color. The right tonsil was enlarged and cryptic.

The folds on the right side of the face were smoothed out. When the lips were retracted, the face was drawn to the left. The eyes closed normally and the forehead wrinkled symmetrically. There were no enlarged cervical glands, tracheal tug or stiffness or retraction of the neck.

As regards the lungs, a slight dulness was obtained at the bases posteriorly. Here also a few crackling and moist râles were heard. The heart and peripheral vessels were not remarkable. The systolic blood pressure was 105 and the diastolic 60. Abdominal examination showed no positive observations. A rectal examination gave negative results.

Observation gave one the impression that the right arm was used more freely than the left. In raising both arms above the head, the left arm was raised higher than the right and was held there longer. The right arm showed more spasticity than the left, and a marked pronator sign was present. The reflexes were not obtainable, as the patient would not relax the arms. The right foot was rotated outward to an abnormal position. The knee reflexes were hypo-active, the left being more so than the right. The ankle jerk was abolished. Slight bilateral Kernig and Babinski signs were present. The abdominal reflexes could not be obtained. Only the right cremasteric reflex was present.

Neurologic Examination (by Dr. LaSalle Archambault).—The pupils were small, equal and regular and reacted to light. The retinal veins were congested with the physiologic cupping of the disks apparently absent. This was more marked on the left side. There was a paralysis of the right lower facial muscles. A slight rigidity of the neck was present. The tongue was not protruded very well, but seemed to deviate to the right. The patient did not talk nor did he make an effort to do so like the ordinary aphasic person; therefore, the question of psychic mutism should be considered.

The pronator sign was present on the right. Bicipital, tricipital and radial jerks were present but hypo-active. Voluntary movements were poorly executed, but the left arm was moved more freely than the right. When the left arm was raised upright by the examiner, the patient had a tendency to maintain it in this position

for some time (catatonia). The right foot was rotated outward to an abnormal degree. Voluntary movements of the legs were rare. Limited movements could be performed equally well with either limb. The knee reflexes were hypo-active, but the left was more active than the right. A bilateral Babinski and a slight bilateral Kernig sign could be elicited. The ankle jerks were absent.

Diagnosis.—The impressions were that the physical signs pointed to a localized left cerebral lesion, involving the motor area. The history of the accident led one to believe that the lesion might be either a meningeal hemorrhage or a subdural extravasation of cerebrospinal fluid. However, a preexisting glioma into which a hemorrhage occurred as a result of the accident was considered and could not be ruled out.

Laboratory Tests.—The complement-fixation test for syphilis on the blood and spinal fluid was negative. No increase in globulin was shown by Noguchi's butyric acid test. The cell count of the spinal fluid was 2 cells per cubic millimeter. Spinal fluid sugar was 93 mg. per hundred cubic centimeters. The results of urinalysis were not remarkable. Roentgen examination showed the sutures and vascular markings of the skull to be normal, with no roentgen evidence of increased intracranial pressure.

Course.—After admission, the patient showed no improvement and had an attack of projectile vomiting. The pulse was slow, sometimes reaching 35. He was operated on by Dr. Arthur H. Stein, who made a subtemporal decompression. Exploration of the left motor area revealed what appeared to be a subcortical tumor not amenable to surgical removal. He did poorly postoperatively and never regained consciousness.

Necropsy.—The examination, performed one-half hour after death, was limited to the head. The body, 176 cm. long, was that of a middle-aged white man, well developed and nourished. Except for the incision made for the decompression, there were no other external marks. Underneath the area of the bone elevated the dura was intact, except for a small opening measuring 2 cm. in diameter. A moderate amount of clotted blood was present in the field of operation.

The brain weighed 1,150 Gm. Definite evidence of increased intracranial pressure was shown by the distinct cerebellar pressure cone and the subtentorial herniation of the hippocampal gyri. There was a symphysis of the mesial surfaces of the frontal lobes with some resistance to digital pressure over the posterior portion of the left frontal and adjoining convolutions. After thorough fixation in 10 per cent neutral formaldehyde, a frontal section through the anterior extremity of the left ventricle showed under the rostrum of the corpus callosum a transversely oblong, hemorrhagic tumor, about 2 by 1.5 cm., involving the right more than the left hemisphere. Even at this level there was a definite enlargement of the left hemisphere as compared with the right.

Section in front of the optic chiasm or anterior commissure showed another large hemorrhagic glioma, similar to the one described previously, occupying the cortex of the left motor area. At this level the enlargement of the left hemisphere became definitely noticeable. The section passing through the third ventricle and the posterior limb of the internal capsule showed that the second focus in the left motor area extended backward as a small, round, vascular lesion about 0.5 cm. in size, in the corona radiata. In addition to this, another small focus involved the lateral segment of the left putamen in direct contact with the external capsule. The lateral ventricles were markedly distorted.

Microscopic Examination.—Sections from several of the lesions in various parts of the brain were stained with hematoxylin and eosin and Mallory's phosphotungstic acid-hematoxylin.

All sections showed the process to be a glioma, but with nothing in the histologic picture to indicate that a metastasis had taken place. The tumors undoubtedly had a multicentric origin. The type cell was large, variable in size and shape and of astrocyte morphology. It had coarse glial processes which with similar fibrils from other glial cells, together with many capillaries, made up the stroma. These glia fibrils were numerous, forming a dense but delicate network in which the glia cells appeared almost isolated from one another over large areas. These

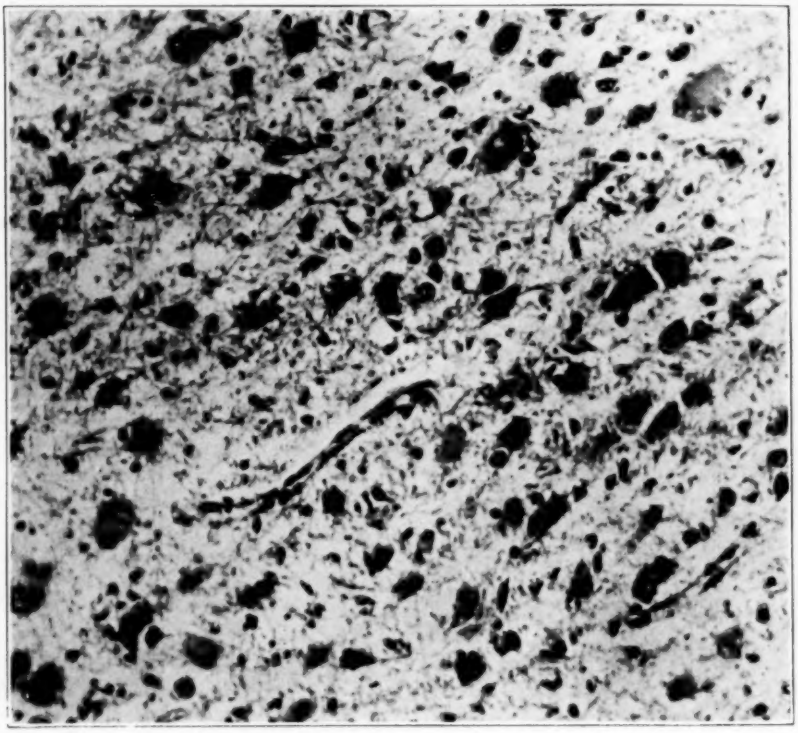

Fig. 1.—Photomicrograph to show the numerous large astrocytes containing one or more nuclei which are generally eccentric. Note the dense network of glia fibrils. Phosphotungstic acid-hematoxylin; × 317.

large cells had an abundant, rather homogeneous, opaque cytoplasm which was very acidophilic (fig. 1). The nucleus was generally round or oval, sometimes crescentic and vesicular and had a prominent nucleolus. The nucleus was generally single (there may be two or even three in any given cell) and frequently eccentric. Mitotic figures were not seen in these cells.

The picture was not uniform, some areas showing a predominant smaller bipolar or apolar cell, with frequent mitotic figures. There were large areas of necrosis and in the adjacent tissue the cells were spindle and closely apposed, with their dark nuclei sometimes in palisade or radiating arrangement around

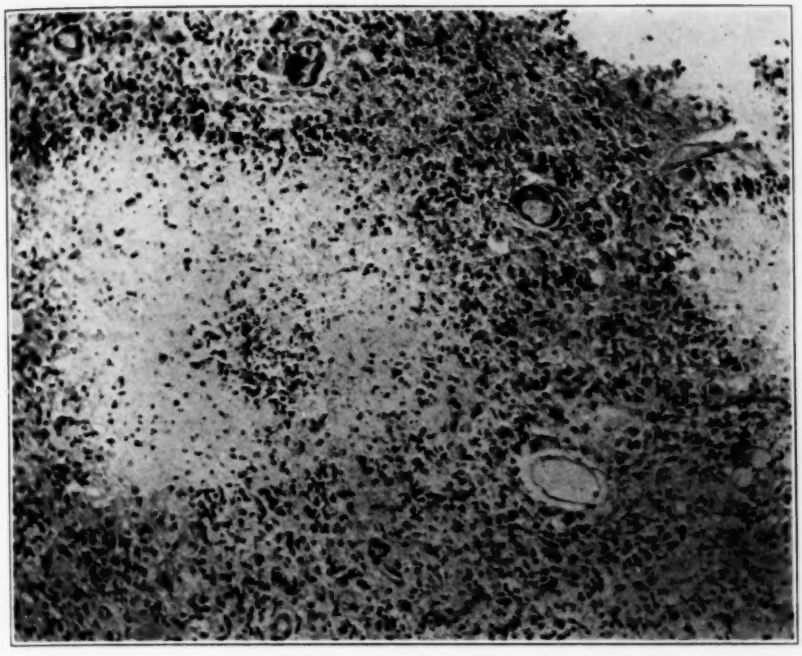

Fig. 2.—Photomicrograph of two of the smaller necrotic areas in one of the gliomas, showing the palisade arrangement of the nuclei around these necrotic areas. Hematoxylin and eosin; × 125.

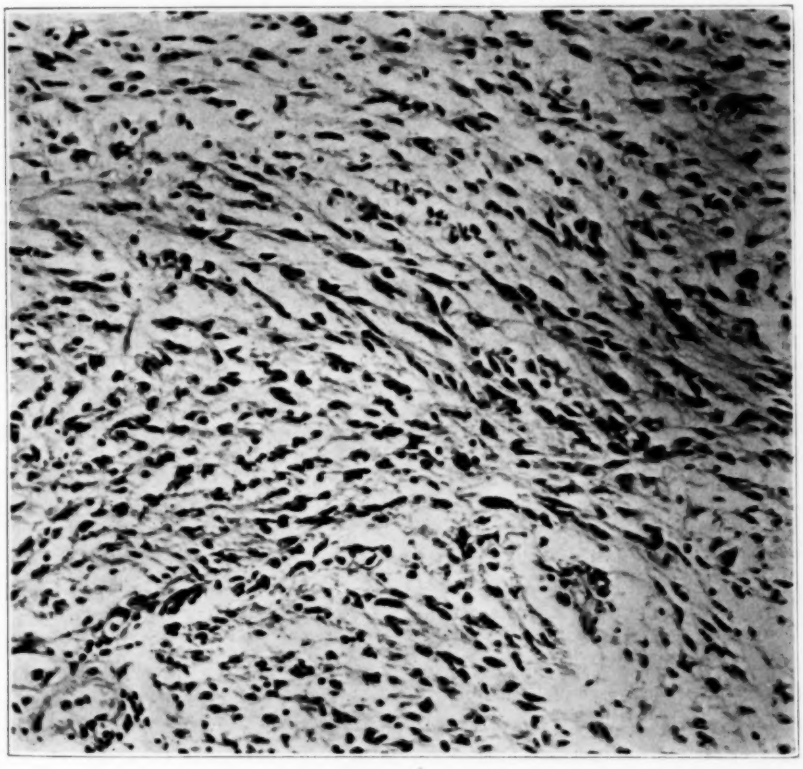

Fig. 3.—Photomicrograph of a spindle cell area from one of the gliomas. Note the general absence of large astrocytes. Hematoxylin and eosin; × 245.

these necrotic areas (fig. 2). In some sections, the spindle cells with their elongated nuclei and glia fibrils predominated (figs. 3 and 4). In certain regions in the tumor area, a number of Nissl's "Staebchenzellen" were present. These were the so-called satellite rod cells so frequently seen in gliomas and other pathologic conditions of the brain. In one section in which the astrocytes were numerous and in which capillaries were not so plentiful, many minute clear cystic spaces were present, illustrative of the cystic degeneration commonly observed in these tumors.

The tumors as a whole were of the fibrillary astrocyte type, but in places showed a more diversified structure. At no point had the new growth reached

Fig. 4.—Photomicrograph of another spindle cell area to show the presence of glia fibrils. A mitotic figure is present in the center of the field. Phosphotungstic acid-hematoxylin; × 562.

the pia. Capillaries showed endothelial and perithelial thickening in the necrotic zones. Those in the near vicinity of these necrotic areas were extensively thrombosed. Even in the non-necrotic areas, a number of the vessels contained a more or less completely occluding thrombus. All of the tumor foci shaded off gradually into the cerebral tissue. The surrounding dense gliosis of the cerebral tissue added to the difficulty of defining the exact limits of the gliomatous process. The cortex overlying the tumor showed a tendency toward neuroglial proliferation in varying degree, being marked in some places, and a peripheral subpial gliosis.

COMMENT

In the necropsy records of the Pathologic Laboratory of the Albany Hospital, from 1917 to 1929, inclusive, there were included twenty-three cases of brain tumors for which complete data are available, distributed as shown in the accompanying table.

This variety of brain tumors is unusual for such a small series. Bailey and Cushing [1] and Bailey,[3] in their large experience of 378 verified gliomas, observed only two examples of double tumors of the glioma series: (1) a pinealoma and a glioma of the optic chiasm; (2) a pinealoma and a medullo-epithelioma. In 1871, Edes [4] reported a case of two gliomas in the parietal and occipital lobes. Bradley,[5] in 1880, described a case of gliomas of the right cerebellum and of the left

Distribution of Brain Tumors

Glioma	
Single	12 cases
Multiple	1 case
Pituitary adenoma	2 cases
Acoustic fibroma	
Unilateral	2 cases
Bilateral	1 case
Meningioma	
Single (with hyperostosis cranei)	1 case
Multiple	1 case
Angioma of cerebral cortex	
Multiple	1 case
Teratoma of cerebellum	1 case
Metastasis from carcinoma uteri	1 case

cerebrum. In 1895, Stroebe [6] reported a large glioma of the right occipital lobe and a smaller tumor nodule under the cortex of the anterior part of the paracentral convolution. Among 127 verified gliomas, Tooth [7] found a case of multiple gliomas (one in each frontal lobe) and another in which a single occipital glioma was associated with

3. Bailey, P.: Further Remarks Concerning Tumors of the Glioma Group, Bull. Johns Hopkins Hosp. **40**:354, 1927.

4. Edes, R. T.: Morbid Growths Connected with the Nervous System; Cerebrum, Cerebellum, Semilunar Ganglion of the Sympathetic, Am. J. M. Sc. **61**:87, 1871.

5. Bradley, W. L.: Case of Glio-Sarcomatous Tumors of the Cerebrum and Cerebellum, Proc. Connecticut M. Soc. **2**:39, 1880.

6. Stroebe, H.: Ueber Entstehung und Bau der Gehirngliome, Beitr. z. path. Anat. u. z. allg. Path. **18**:405, 1895.

7. Tooth, H. H.: Some Observations on the Growth and Survival Period of Intracranial Tumors Based on the Records of 500 Cases with Special Reference to the Pathology of the Gliomata, Brain **35**:61, 1912.

an angiosarcoma of the right marginal gyrus. In Froehlich's case,[8] three gliomas were present in the left cerebral hemisphere. In a pathologic study of forty intracranial tumors. eleven of which were gliomas, Greenfield[9] reported a case of multiple gliomas of the brain stem and cord, another of a glioma and a spongioblastoma and finally one of multiple gliomas of the intracranial nerve roots. As no detailed descriptions were given in the cases of Greenfield, one cannot say whether this multiplicity of tumors was primary or secondary. Giannuli[10] described a glioma of the right parietal lobe and of the pons. In Freeman's case,[11] the three gliomas were located in the left frontal pole, genu of the corpus callosum and the left frontal operculum. Of a total of about fifty-one gliomas, Purves-Stewart[12] found two separate gliomas in one brain, symmetrically situated in each cerebral hemisphere.

As mentioned previously, I believe that the multiple gliomas in the case reported are of multicentric origin and not due to a metastatic process. In this case, the meninges and those portions of the brain tissue bathed by the cerebrospinal fluid were not involved. In fact, the absence of metastasis in gliomas in general is remarkable. Bailey and Cushing, in discussing the spongioblastoma multiforme, not only the largest single group in the glioma series but one of the most malignant, stated that this tumor does not metastasize nor rarely if ever inoculates the meninges; the medulloblastoma, probably no less malignant than the spongioblastoma, not infrequently disseminates itself through the subarachnoid spaces. Councilman[13] attributed the absence of metastasis to the absence of lymphatics and to the tendency of noninvasion of blood vessels by the tumor cells. According to the anatomist Testut,[14] true lymphatic vessels are not found in the brain. Mallory[15] stated that although glioblastomas often show a marked tendency to infiltrate the tissue surrounding them, they apparently do not invade blood vessels.

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8. Froehlich, E.: Ein Fall von multiplen Gliomen, Deutsche med. Wchnschr. **41**:951, 1915.

9. Greenfield, J. G.: The Pathological Examination of Forty Intracranial Neoplasms, Brain **42**:29, 1919.

10. Giannuli, F.: Glioma de parieto-pontino dell emisfero cerebrale destro, Policlinico **33**:281, 1926.

11. Freeman, W.: Reactive Gliosis in a Case of Brain Tumor, Arch. Neurol. & Psychiat. **14**:649 (Nov.) 1925.

12. Purves-Stewart, J.: Intracranial Tumors and Some Errors in Their Diagnosis, London, Oxford University Press, 1927, p. 206.

13. Councilman, W. T.: Anatomical Consideration of Tumors of the Brain with Special Reference to the Gliomata, Colorado Med. **12**:289, 1915.

14. Testut, L.: Traité d'anatomie humaine, Paris, Octave Doin et Fils, 1911, vol. 12, p. 949.

15. Mallory, F. B.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1918, p. 677.

Uyematsu [16] found that the proliferating glioma does not progress in the direction of the least resistance nor does it grow by way of the lymph channel or blood stream, but in most cases there is a very gradual transition into the surrounding brain substance.

That regional metastases may occur within the central nervous system by way of the cerebrospinal pathway is indicated by the few cases reported in the literature. In Leusden's case,[17] a glioma of the lumbar enlargement metastasized to the left lateral ventricle, besides infiltrating the leptomeninges of the spinal cord and of the base of the brain. Fraenkel and Benda [18] reported a case of glioma of the fifth dorsal segment and another of ependymoma of the ninth dorsal segment of the spinal cord, in both of which the pia was secondarily involved at all levels of the cord. In one of Henneberg's cases,[19] a glioma of the pons and medulla was associated with multiple gliomatous nodules of the lateral ventricles. He [20] reported another case of multiple ependymal gliomas of all four ventricles of the brain which he believed originated in situ but which may be considered as metastatic probably from the largest tumor, the size of a hen's egg, filling the fourth ventricle. Mallory [15] mentioned a typical glioma over the coccyx in a woman, aged 42, which recurred after removal and gave rise to metastases in both inguinal lymph nodes. Spiller [21] reported an ependymoma of the fourth ventricle which produced a small metastatic tumor nodule on the lower part of the thoracic region of the cord as well as an extension down on the cord to the sixth cervical segment. In Schupfer's case,[22] a glioma of the right temporal lobe extended out over the base of the brain and produced multiple metastases in the spinal pia-arachnoid. In the case reported by Stumpf,[23] the cerebellar glioma produced a metastatic tumor

16. Uyematsu, S.: A Contribution to the Study of Glioma, J. Nerv. & Ment. Dis. **53**:81, 1921.

17. Leusden, P.: Ueber einen eigenthuemlichen Fall von Gliom des Rueckenmarks mit Uebergreifen auf die weichen Haeute des Rueckenmarks und Gehirns, Beitr. z. path. Anat. u. z. allg. Path. **23**:69, 1898.

18. Fraenkel, A., and Benda, C.: Zur Lehre von den Geschwuelsten der Rueckenmarkshaeute, Deutsche med. Wchnschr. **24**:442, 457 and 476, 1898.

19. Henneberg, R.: Ueber Ventrikel- und Pons-tumoren, Charité-Ann. **27**:493, 1900.

20. Henneberg, R.: Ueber das ependymaere Gliom, Berl. klin. Wchnschr. **42**: 1318, 1905.

21. Spiller, W. G.: Gliomatosis of the Pia and Metastasis of Glioma, J. Nerv. & Ment. Dis. **34**:297, 1907.

22. Schupfer, F.: Ueber einen Fall von Gliosarkom im rechten Schlaefenlappen mit ausgedehnter, einen grossen Teil des Rueckenmarks umguertender Metastase, Monatschr. f. Psychiat. u. Neurol. **24**:63, 1908.

23. Stumpf, R.: Histologische Beitraege zur Kenntnis des Glioms, Beitr. z. path. Anat. u. z. allg. Path. **51**:1, 1911.

in each of the lateral ventricles. Schaede [24] reported a case of cerebral glioma of the astrocyte type which involved the right lateral ventricle and developed multiple metastases of the spinal pia. Mees [24a] described a glioma of the fourth cervical segment which produced many metastatic nodules on the pons and medulla and left frontal pole, and an extension down the entire length of the cord. In Lahmeyer's case,[25] there was a glioma of the brain and another, well developed, in the thoracic spinal cord which infiltrated the pia along the entire length of the cord. In Schmincke's case,[26] in addition to the primary cerebellar glioma, smaller tumor masses were found in the lateral ventricles, central canal of the cervical spinal cord and the nerve trunks of the cauda equina; the leptomeninges of the pons and of the entire cord were infiltrated with tumor cells. It is difficult to state how much of this is due to metastasis and how much to direct extension. It is to be noted that in this case tumor cells were present lying free in the central canal of the cervical cord. In the similar case of Jacob,[27] the cerebellar glioma extended into and obliterated the third and fourth ventricles and the central canal of the spinal cord with metastasis to the lateral ventricles and leptomeninges. Mueller [28] reported a case of multiple gliomas of the brain and spinal cord, all of which he considered as primary, but some of which must be looked on as metastatic, since groups of tumor cells were present in the meshes of the pia-arachnoid. So far there is no definitely proved case of distant metastasis to the various extracranial viscera from a glioma primary in the central nervous system. In 1897, Moeller [29] reported a case of gliosarcoma of the spinal cord with metastasis to the lung, small intestine and right suprarenal medulla. His microscopic description was meager and phosphotungstic acid-hematoxylin was not used as a differential stain. One wonders whether the growth was not a sympathicoblastoma primary in the suprarenal medulla with central metastasis, for it is now well known that such

24. Schaede, G.: Ueber diffuse Geschwülstbildung in der Pia mater, Ztschr. f. d. ges. Neurol. u. Psychiat. **6**:96, 1911.

24a. Mees, R. A.: Ein röhrenförmiges Gliom des Rückenmarkes mit regionären Metastasen, Ztschr. f. d. ges. Neurol. u. Psychiat. **9**:463, 1912.

25. Lahmeyer, F.: Ein Fall von Geschwülstbildung im Gehirn und in den weichen Haeuten des gesamtem Zentralnervensystems, Deutsche Ztschr. f. Nervenh. **49**:348, 1913.

26. Schmincke, A.: Ein glioblastisches Sarkom des Kleinhirns mit Metastasenbildung im Hirn und Rueckenmark, Frankfurt. Ztschr. f. Path. **16**:357, 1915.

27. Jacob, F. M.: Glioma of the Cerebellum with Metastases, J. M. Research **34**:95, 1916.

28. Mueller, H. W.: Ueber multiple Gliome im Gehirn und Rueckenmark, Schweiz. med. Wchnschr. **54**:1107, 1924.

29. Moeller, C.: Ein Fall von Gliosarkom des Rueckenmarks mit Metastasen in Lunge, Darm und Nebenniere, Deutsche med. Wchnschr. **23**:306, 1897.

suprarenal tumors were described as sarcomas and gliomas before Wright's [30] important summary of the subject in 1910.

In addition, gliomas have been known to extend along surfaces for great distances. Firor and Ford,[31] and more recently Brannan,[32] have made excellent reviews of the reported cases of secondary gliomatosis of the pia-arachnoid due to extension or metastasis, or both, bringing the total to eighteen cases. Among others, the cases of Loehe,[33] Councilman, and Viets [34] were not included in their reports. In Loehe's case, a glioma of the pons extended in a diffuse manner up over the convex surface of the brain and down over the spinal cord. Councilman reported three interesting cases illustrative of the manner of extension along the subarachnoidal spaces. In the first case, a pontile glioma grew over the pons in a manner much resembling a mass of plaster poured over its surface. In the second, a glioma of the cerebellar cortex extended over the surface of the cerebellum and along the entire length of the cord, which was slightly infiltrated by the tumor cells. Lastly a glioma located in the frontal lobe grew both in the brain and out into the arachnoid and extended over the first frontal convolution almost to the longitudinal fissure. A remarkable case was observed by Mallory [35] in which a glioma, originating in the lumbar region of the spinal cord, enveloped and infiltrated the entire cord and grew over the cerebellum and cerebral hemispheres. In Viets' case, a glioma of the right temporal lobe extended to the base of the brain and bulb where it ran in the subarachnoid spaces over a large part of the ventral surface of the brain and extended down the spinal cord to the conus terminalis without invading any part of the central nervous system except a small portion of the left cerebellum.

Among the thirteen cases of gliomas listed, there was one of medulloblastoma of the cerebellum in which the cerebellar hemispheres were completely enveloped by the tumor cells; grossly, the meninges were thickened and opaquely white like that of a marked chronic lepto-

30. Wright, J. H.: Neurocytoma or Neuroblastoma: A Kind of Tumor not Generally Recognized, J. Exper. Med. **12**:556, 1910.

31. Firor, W. M., and Ford, F. R.: Gliomatosis of the Leptomeninges, Bull. Johns Hopkins Hosp. **35**:108, 1924.

32. Brannan, D.: Secondary Gliomatosis of the Leptomeninges, Am. J. Path. **2**:123, 1926.

33. Loehe, H.: Zwei Faelle von Metastasenbildung boesartiger Geschwuelste in der Leptomeninx, Virchows Arch. f. path. Anat. u. Physiol. **206**:467, 1911.

34. Viets, H.: A Note on Gliomata with Report of a Case, Boston M. & S. J. **184**:150, 1921.

35. Mallory, F. B.: The Result of the Application of Special Histological Methods to the Study of Tumors, J. Exper. Med. **10**:575, 1908.

meningitis. Strassner [36] described a diffuse extramedullary gliomatosis of the spinal pia which in several places infiltrated the thoracic spinal cord and the conus medullaris. In this case, no primary glioma of the brain or spinal cord was found. In the light of present knowledge, the unusual case reported by Bruns,[37] in 1896, as sarcoma may be regarded as a glioma of the lumbar cord, the intramedullary portion of which extended to the level of the midthoracic cord while the secondary gliomatosis of the meninges reached the level of the upper dorsal cord.

Much has been written about trauma as an etiologic factor in the production of gliomas. No definite experimental proof has as yet been offered. In the case here reported, the automobile accident may be interpreted as precipitating the acute symptoms of increasing intracranial pressure through hemorrhage into the gliomas, which was demonstrated at necropsy. It should be noted here that before the accident the patient had been worrying needlessly, was irritable at times and had expressed the ideas that his head felt queer and he was afraid he would lose his mind.

That interesting and unique accompaniment of gliomas—a generalized gliosis of the brain—not found to any comparative degree in other intracranial tumors, has elicited much comment on the part of many observers. The gliosis of the brain in my case is much more in evidence than in cases of involvement of the brain with lesions of any magnitude—extensive brain abscess, multiple dural meningiomas, multiple angiomas of the cerebral cortex, teratoma of the cerebellum associated with massive internal hydrocephalus—which I restudied for comparative purposes. Uyematsu, who made a special study of this aspect of generalized neuroglial proliferation in gliomas, in his critical review of the literature up to 1921, concluded that a congenital predisposition was at work, producing both the tumor itself and this abnormal proliferation of neuroglia cells. In a case of multiple gliomas of the frontal lobe, Freeman found that in sections from the temporal and occipital lobes the number of neuroglia cells was always definitely increased by actual counts on the side of the lesion, although no differences in their sizes were appreciable.

In view of the origin of gliomas from cells of the neural canal or from their derivatives, the neuroglia cells, it may be interesting to note the various locations where they are likely to occur. Mallory stated that gliomas occur only within the central nervous system and its outgrowths and from the remains of the neural canal over the coccyx and

36. Strassner, H.: Ueber die diffusen Geschwuelste der weichen Rueckenmarkshaeute mit besonderer Beruecksichtigung der extramedullaeren Gliomatose, Deutsche Ztschr. f. Nervenh. **37**:305, 1909.

37. Bruns, L.: Klinische und pathologisch-anatomische Beitraege zur Chirurgie der Rueckenmarkstumoren, Arch. f. Psychiat. **28**:97, 1896.

at the base of the nose where closure of the canal takes place and where atrophy and disappearance of the ependymal cells are often incomplete. One must bear in mind that not all nasal gliomas are primary, as shown in the unique case of Guthrie and Dott,[38] in which a left inferior frontal spongioblastoma produced an intranasal protusion by direct penetration through the cribriform plate. Similarly, an abdominal glioma may be of central origin, as shown by the remarkable case of Fischer,[39] in which the growth in the lumbar cord had eroded into the abdominal cavity. Typical primary gliomas over the coccyx and buttocks or in the nose have been reported by Mallory,[40] Kimpton [41] and Clark.[42] Among nineteen verified ventral tumors of the sacrum, Hundling [43] found five cases of ependymal glioma. Gliomas in these unusual locations are obviously congenital.

In my case, the multiplicity of the tumors combined with the generalized neuroglial proliferation, not observed to a comparative degree in other cases of extensive involvement of the brain, would appear to point to a congenital influence as an etiologic factor.

SUMMARY

A case of multiple gliomas of the cerebrum is reported, with physical signs pointing chiefly to a left cerebral lesion and involving the motor area. Trauma precipitated the onset of acute symptoms of progressing intracranial pressure, owing to hemorrhage into the gliomas. Microscopically, the three gliomas were of the fibrillary astrocytoma variety. There was associated a generalized gliosis in the brain substance.

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38. Guthrie, D., and Dott, N.: The Occurrence of Brain-Tissue Within the Nose: the So-Called Nasal Glioma, J. Laryng. & Otol. **42**:733, 1927.

39. Fischer, O.: Arch. f. Heilk. **22**:344, 1901; cited by Firor and Ford: Bull. Johns Hopkins Hosp. **35**:108, 1924.

40. Mallory, F. B.: Three Gliomata of Ependymal Origin: Two in the Fourth Ventricle, One Subcutaneous Over the Coccyx, J. M. Research **8**:1, 1902.

41. Kimpton, A. R.: Glioma of the Buttock, Ann. Surg. **70**:582, 1919.

42. Clark, J. P.: Glioma of the Nose: Report of Two Congenital Cases, Am. J. M. Sc. **129**:769, 1905.

43. Hundling, H. W.: Ventral Tumors of the Sacrum, Surg. Gynec. Obst. **38**:518, 1924.

PSYCHOLOGY AND HYSTERIA*

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There are many subjects in medicine that are quite clear as long as one has to handle the separate cases in practice. But if one sits down to explain them they become confused in many aspects. Hysteria is one of these subjects. Since Charcot described the different symptoms of this illness, it has become a recognized part of medicine. One can now diagnose special symptoms as hysterical and know that no physical reason for them can be found. So far, everything is clear.

But if one asks for an explanation of the symptoms, and especially for an explanation which would enable one to treat them with success, the matter becomes very complicated. Charcot himself believed that a special form of degeneration of the nervous system was the cause of hysteria. But he failed to indicate what that form was. The same explanation was used for many other neuroses and psychoses and so became a cloak for ignorance. The studies of Liébault and Bernheim on the influence of suggestion in hysteria, which Charcot had discovered, led the way to a more psychologic explanation. This was elaborated chiefly by Pierre Janet. He pointed out that the degeneration causing hysteria consists of a mental weakness, an inability to unite different contents in consciousness, and that suggestibility arises from this weakness of the "perception personelle." To others, such as Babinski, the suggestibility in itself is an indication of hysterical degeneration of the mind. On the whole, French psychiatrists tend to accept an inborn defect of character as the cause of hysterical symptoms.

This is not so in Germany. There the explanation of hysteria has developed in a different way. German psychiatrists, such as Moebius, expressed the opinion that emotion forms an essential part of the hysterical reaction, and this view of the hysterical symptom as an abnormal expression of emotion became the central point with German psychiatry.

Emotions may express themselves in different ways, and those expressions tend to become abnormal under certain conditions. The opinion was expressed, first by Moebius and Hoche, later by many other psychiatrists, that any one may show hysterical symptoms under difficult circumstances. The hysterical reaction takes a different form from the ordinary emotional reactions because it is of a primitive kind.

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Gaupp and Kraepelin defended the supposition that these primitive reactions can arise in all of us, that they show themselves sooner in primitive people (for example, country girls serving in the city) or under unusually exciting conditions, and that the only difference in liability to these symptoms lies in the greater or less resistance of the personality.

But the questions remain: What circumstances weaken this resistance, and how does it happen that many hysterical reactions take such curious forms? Much valuable work has been done to explain the mechanism, or, as I like to say, the psychism, of the hysterical reaction. I may remind you of Kretschmer's study of the fixation of symptoms of shell shock into hysterical reactions. The psychism of the symptoms has been clarified most, however, by the work of Freud. The essential part of his opinions has now been accepted by a great many psychiatrists. The hysterical psychism may be briefly sketched thus:

First, a primitive or abnormal emotional expression occurs, either because a normal expression has not been developed (modern war, sexuality in childhood) or because it has been suppressed for special reasons. Second, this abnormal expression becomes fixed, because it still gives some expression to an emotional tension, or because secondary advantages result. Third, the fixed expression becomes the usual one for that emotion in certain situations. This meaning of the symptoms, which can be explained from their history, remains unconscious to the patients themselves and can be studied only by long and careful analysis of their histories. But if one spends enough time and energy on this analysis, one will often be able to learn the cause of hysterical symptoms that may seem incomprehensible from a less thorough examination.

To some adherents of Freud, it seems that one needs no other factor to explain all hysterical cases and that if one fails to do so, it is because of resistance or because of faults in the analysis. Most investigators, however, and Freud among them, agree that some inborn factors are of importance as well. Otherwise it is not clear why hysterical symptoms sometimes take such a special place in the structure of the character. In some cases these symptoms seem incidental; in others, like war hysteria, a few symptoms dominate the whole behavior, and in other patients, all kinds of psychic traits form the "hysterical character."

The question arises whether there is a certain more or less specific psychic disposition that would explain such developments of hysterical symptoms. Here one is nearer to the French conception of hysteria as an inborn defect of character. Yet the way of approach is different, because one need not explain everything from this structure of the character. One can formulate the question thus: Is there a special

type of character, or are there different types in which the hysterical psychism finds special opportunity to develop into more elaborate forms?

Here I come to my own conception, which has been much influenced by that of Jung. In his book on psychologic types Jung stated that hysteria is the most frequent neurosis in extroverted types, and that one finds it most of all in extroverted feeling types. He has not made it entirely clear why this should be. In my opinion, he tries to explain too much by extroversion. This problem of the relation between types and certain forms of neurosis has interested me ever since I learned of the conception of the types (which was about the time of their first formulation by Jung). I now have gathered a material of 150 cases from my own practice in which it was possible to see the structure of the neurosis in relation to the eight types and to the many forms of neurotic complexes, and this enables me to answer certain questions in a preliminary way.

I find that hysterical symptoms may be observed in persons of very different types. So far I agree with the opinion prevailing among German psychiatrists. But I can also confirm Jung's statement that both extroversion and the predominance of feeling tend to give the hysterical expression a greater influence in a person's psychology. I shall try to explain why this is the case and how these factors affect hysterical symptoms.

I shall begin with feeling, because this is the most difficult factor to explain. The term is often used in a very vague sense, and to many psychologists feeling and emotion mean the same thing. Now I oppose feeling, or sentiment, and emotion, and I think that this may be the best point from which to start for an explanation. This also is a point in which I differ from Jung and in which I am much nearer to psychologists like Shand or McDougall. They also distinguish between the emotional expression, which belongs to instinct, and sentiment (which I consider to be synonymous with feeling) which means "an organized system of emotional tendencies centered about some object." Emotion is an element of feeling, but the latter forms a structural unit which is not to be found in the emotional expression as such. An example may make this clearer. I am walking through a crowded street in a hurry, and I collide with another person. My first reaction may be anger. Then I see that it is a small child that is in front of me, and a tender emotion, a fatherly, protective instinct may be aroused. From these contradictory emotions a sentiment may arise of wanting to guide this child into a safer place. A feeling or sentiment is not one reaction only, but more, a certain mental attitude toward a subject, and this attitude may be very complex. Yet all these different emotional parts have their proper place in the attitude. Such a plastic attitude, expressing different reactions in one unit, seems to me the

essence of feeling or sentiment. McDougall contrasts sentiments like reproach, shame and sorrow, with simple emotions like fear, anger and curiosity. Another approach may be to consider the complicated attitudes that develop in a child toward persons in its surroundings. Freud has shown clearly how such feeling attitudes, for instance, toward father or mother, develop a great independence, and how they may be transferred to other people again and again, even though there is little objective reason for it. Such attitudes are not simple emotions; they are complex sentiments.

Such sentiments occur in every person, and they are of the greatest importance in our relations with other people. One may even say that feeling or sentiments have a certain objective value. Under given circumstances, we all try to adopt the right attitude. Yet this influence is not dominating in every one. With some, however, it is, and then one may speak of a person of the feeling type. To these persons, it is of the utmost importance that they find the right attitude in every circumstance, and that the relation with other people should correspond to their ideals. They have a talent for developing and differentiating feeling attitudes and for giving the right response to the attitudes of others. Therefore, persons of the feeling type have a much greater stability, plasticity and subtlety in their emotional expressions than persons who are merely emotional. Often this is of great advantage in human relations, but sometimes faulty attitudes may become fixed, and may prove very obstinate.

One may ask what influence the prevalence of feeling has on the psychism of hysterical symptoms. We have seen that hysterical symptoms mean emotional expressions fixed in abnormal forms. But all kinds of emotional expressions are being canalized into feeling attitudes by the feeling type. So, as a rule, one ought to expect hysterical expressions less here. On the other hand, it may happen that special emotions cannot be brought together into the system of feeling attitudes that directs the life of a person of the feeling type. Then such a situation is much more traumatic to persons of this type than to others. Hence repression may become of great importance in order to maintain mental balance, more so than with others. The influence of such traumatic experiences may thus be increased. One can see this influence in small children. Freud asked himself why certain children proved especially apt to experience sexual traumas, why these traumas had a much greater influence on them, or why they even invented them and made fantasies about them. Freud came to the conclusion that an inborn factor of precocity of sexual instincts might be a factor. But I have the impression, from my experience, that although this may be partly true, the predominance of feeling in such children may be of great influence as well in causing the elaboration of

such experiences. One may find this same influence in later life with persons of this type. The fact that no harmonious attitude can be found toward a situation acts in a much more lasting and disturbing way in such persons. When an inner conflict occurs in the emotional life, it tends to influence the whole feeling life.

As long as the resistance is strong enough to repress the conflict, nothing appears on the surface, but when a hysterical symptom arises —there is nothing special for the type in the symptoms as such—the reaction of the feeling type is remarkable. One can distinguish three kinds of hysterical reactions: (*a*) crises, (*b*) conversion symptoms, (*c*) psychic reactions. In hysterical crises, the patient loses control of his primitive emotional expressions. To people of the feeling type this is more dangerous than to others, because it is so much in conflict with their ideals, and because this kind of expression may easily develop into a kind of manifestation (for instance, of protest) with them. In conversion symptoms, the attitude of being ill, of wanting to be pitied and petted by others, may come to dominate all expressions of feeling. The tendency of the feeling type to develop his feeling attitudes more and more is most strongly emphasized in the psychic symptoms of hysteria. These symptoms are emotional reactions which may easily be seen to be in contrast with the ideals to which these people try to direct themselves consciously. Such reactions, too, when they are more or less admitted to consciousness, tend to develop into feeling attitudes with feeling types, but it is impossible to unite them with other feeling expressions into one harmonious whole. The result is a disturbance of the mental equilibrium showing two different forms. The hysterical patient may try to ignore the fact that the unity of his feelings has been confused. He keeps up the appearance of unity. But the conflicts, which cannot be entirely hidden, cause an inner unrest which has to be overruled by artificial means. To others, this may look like dishonesty and pose. A second reaction of the personality is that the certainty of the principal function is lost, and a kind of paralysis of feeling results. A depression then arises, often accompanied by feelings of guilt. These two reactions may also occur alternately. The first form, however, is more often found in persons of the extrovert feeling type, the second in persons of the introvert feeling type.

I can be more brief in explaining the influence of extroversion on hysterical symptoms. Introversion and extroversion have become well known to psychiatrists as factors causing certain psychologic accents. All persons have both forms of adaptation, to the outer world, and to their own personal needs; yet one side is usually more developed in conscious motivation. The extrovert is directed toward the outer world, and the inner courses of his behavior are but little known to him. The introvert notes distinctly what he thinks, feels and wants, but he is much less certain about other people and about circumstances.

The influence of the predominance of extroversion on hysterical symptoms is different from the influence of the feeling function. The latter makes the hysterical symptoms a part of the personal expression, whereas extroversion causes the symptoms to remain unchanged and to form certain alterations in the relation with the outside world. If a hysterical reaction occurs, the extrovert looks naturally for causes in the outside world or, at the most, in his own body. He does not understand that a conflict of wishes may bring about a pathologic expression. He seeks to avoid the disturbance by extroversion, in which he feels at home. All the circumstances that have led to his reactions must be avoided or changed. They are the cause, not he. The hysterical reaction has to be explained in such a way that it does not disturb the relation with the surroundings. To others, it may appear, however, that there must be more behind it. If one can study the fantasies of such people, these reactions become much easier to understand. Often, however, they are either not conscious of their fantasies, or they regard them as a sphere quite apart from their ordinary life. Whereas most extroverted people succeed in running away from hysterical symptoms and, if only temporarily, getting rid of them, this is not easy for feeling extroverts, because feeling tends to make these symptoms a part of the personal expression. Hence feeling extroverts are the people in whom such reactions may have the greatest influence on the whole of their lives and personalities. They may become so-called "hysterical characters." But I wish at once to make the point that one cannot consider the hysterical character simply as an exaggeration of the extrovert feeling type. Healthy people of this type have nothing to do with hysteria. The hysterical psychism is necessary as a pathologic addition. If this is the case, however, the psychism may easily acquire an enormous influence. If an important part of the emotional life is being suppressed, as in the hysterical psychism, then there occurs a sphere of emotional tension in which the feeling function cannot exercise its ordinary influence. If repression does not succeed entirely, and especially if the suppressed contents express themselves in the psychic sphere, it becomes evident that the conscious ideals of human relations cannot be maintained under all circumstances. The extrovert feeling type will not admit this, lest all sense of security be lost. The usual form of adaptation now has to serve a second purpose. It is used to cover up the conflict. Thus an exaggeration of the principal function arises by the attempt to compensate for the feeling of uncertainty and inferiority. The feeling contact with the surroundings may be used with virtuosity to create an impression that everything is all right. The feeling of inferiority thus causes a wish to be considered the ("Geltungsbedürfnis" of Kurt Schneider). If the hysterical reactions increase (for instance through traumatic circumstances or

through lack of emotional satisfaction), other people may notice expressions (for instance, infantile sexuality or malice) that are in contrast with the ideals consciously proclaimed. This creates an impression of dishonesty and pose (Bumke). The clearer this contrast, the more the behavior of the hysterical patient becomes a pretence and impresses others as being theatrical. Such a patient may then try to convince others by making scenes. Noticing, however, that the contact with the surroundings is weakened and that many turn away from her, the patient's confidence in the expression of her feelings becomes shaken. She withdraws from people, becomes apathetic, turns to her fantasies, gets into dream states and neglects all adaptation ("Egocentrizität, Unfähigkeit zum Du-erlebnis," Kahn). This is worse for her since, as an extrovert, her more vital and fruitful relations were those with the outside world. The patient's relations with the inside world are vague and fantastic, and she cannot bring them into order. Pathologic conditions of introversion with intense fantasies may then alternate with violent attempts to convince others through exaggerated expressions of feelings. The original adaptation is spoiled by exaggeration and by the influence of fantasy, and in the end it is used only to give expression to complexes. Thus the development of the hysterical reactions into the hysterical character and this special form of hysterical degeneration have their origin in the interaction between hysterical psychism and extrovert feeling adaptation.

It seems to me that this way of regarding the hysterical character enables one to see the relation with the hysterical symptoms more clearly. Kahn has shown in a recent study of the subject that the hysterical reaction and the hysterical personality are two wholly different phenomena. Although it may be true that as a rule one finds many hysterical reactions by people of an hysterical personality, yet the latter may sometimes show no symptoms at all or only at rare intervals. But they can still be characterized by their general psychic attitude (seelische Gesamthaltung). Kahn says that one might speak of an "hysterical character without hysteria" in such a case. I quite agree with his views, but I think that the relation can be explained in a better way.

I once treated such a patient by psychoanalysis, and the structure of the disturbance became very clear to me. There were practically no hysterical symptoms in this case. The woman, then aged about 27, came to me because she had difficulties with her general adaptation, and with her work in a school for social workers. After some time, it was discovered that she was a feeling extrovert, and that her feeling function was divided into two opposing parts. There had been a fundamental trauma when she was 4 or 5 years of age. At that age, a young gardener seduced her to sexual manipulations. After some time she stopped, but her fantasy was much aroused by these events. Her parents were rich, conventional, more or less idle people of orthodox religion. Now her

feelings developed in two different spheres, one respectable and religious, one sexual and connected with the simple life of the working people. It was a curious thing to notice how much all forms of manual labor were related with sexual problems and with the conflict of the two spheres. The sexual side developed mostly into fantasies, and these paralyzed her adaptation in society and made her react in a "hysterical" way. She did not make the impression of a feeling extrovert, because her inborn tendency of adaptation had become unserviceable on account of the inner conflict of the two spheres. That the feeling contact with others formed her principal form of expression was shown by her inability to develop other forms, and by her conduct after recovery. Her own form of adaptation has now appeared.

My experience with other patients makes me feel certain that this conflict in the feeling life would not have developed in the same way if the same trauma had happened to another type. The influence of the type on the structure of the disturbance seems to me to be very great in such cases. Yet in other cases it may be so small that one may neglect it altogether. The psychism of the hysterical symptom is the influence that can explain everything in these cases. Thus, one may come to distinguish different forms of hysteria, according to the influence of the different factors of psychism and character type. In all these forms the hysterical psychism is always active.

(*A*) One may consider as a first form those cases in which the psychism is of chief importance. One finds this with monosymptomatic forms of hysteria and in cases in which a severe shock has caused the disturbance and has originated a certain set of symptoms (probably many forms of war neurosis).

A girl, aged 17, suffered from a very loud, constant hiccup that arose without known cause and troubled her for weeks, so that she was brought to the clinic. She had had no previous nervous trouble. Psychoanalytic treatment revealed that the hiccup began after her mother, a widow, told her that she intended to give up her boarding house, and that she and her brothers ought to find work for themselves. She was much shocked, as she was extremely attached to her home, wept passionately and awakened the next day without any memory of the conversation, but with the hiccup. After the problem became conscious, she had difficulty in finding a new adjustment, but after finding it, she became normal again.

(*B*) A second form is caused by hysterical reactions springing from a primitive form of mind. This is also the form found mostly in young children (for instance, at puberty: "Entwicklungshysterie"). Hysterical reactions arise more readily, but they have no fixed form. They vary, and they tend to disappear under better conditions.

A woman, aged 19, recently married and pregnant with her first child, was brought to the clinic, having fainted in a crowd. She had had fainting fits for two months. Previously she had been healthy but emotional. She once jumped into a canal because her husband, a sailor, failed to write to her. On examination, hypesthesia and hypalgesia were found on the left side. Three months

later, she was brought in again in an excited state. She wanted to drown herself. Her husband neglected her. She was living with her family. Difficulties in these relations made it necessary to take her into the hospital two years later, four times within one year. She stayed a short time on each occasion, then went home well again and worked for her living. She had lost two babies; her family reproved her for this, her husband threatened to leave her, and her sister tried to take advantage of her. She responded to this situation with occasional fits of delirium, laughing and crying at the same time, ran away, and made scenes, beating about her and falling to the ground. In a dream state in the clinic she tore her clothes, made tombs for her children out of the fragments and prayed near them.

(*C*) A third form arises out of the interaction of hysterical psychisms with extrovert adaptation. In this form also the symptoms may come and go. The structure of the psychisms is more stable, however, than in the case of primitive people, and the instability of the symptoms is caused by the ability to avoid difficult situations and to explain away conflicts.

A married woman, aged 40, had never found the right contact with her husband; in fact, she never really loved him and realized this only when there were children whom she could not leave. She was an intuitive extrovert and found an outlet for her many talents and great energy in social work. Then she met a man with whom she fell in love. As a result of the inner conflict, a state of mental confusion arose, so that she had to stay in an institution for some time. Her state could be best described as hysteria. When she found her adaptation again, she plunged into new activities. After a few years, a symptom arose that brought her to me. For about a year she suffered from nervous diarrhea occurring after any kind of excitement. Psychoanalysis showed that behind this symptom was hidden a fierce hatred of certain aspects of her husband. After she experienced this situation in a very convincing way, the symptom disappeared. Instead of running away from herself, she faced her inner conflict, accepted more introversion and developed a new form of balance.

(*D*) Fourth, there is the interaction between hysterical psychism and introverted feeling. The symptoms often have a chronic form, and they may be accompanied by a strong depression, by feelings of guilt, by anxiety and by physical exhaustion. Emotional conflicts have a paralyzing influence on the inner life in such cases.

A married woman, aged 31, came to me in a poor state of health, suffering from a severe and constant headache, which remained after an otitis media. No physical cause could be found. She suffered much from depression and was afraid of dying, as a cousin whom she had nursed had died. She was a feeling introvert with a subtle inner life and fine esthetic tastes. Psychoanalysis discovered the following situation: The husband, a thinking type, was very busy, and absorbed by his work, so their contact gradually weakened. Then a cousin of the husband passed a long vacation at their house. They saw much of each other, and she fell in love with him. He contracted otitis media, and she nursed him. He suffered severe headaches, mastoiditis developed, and he died after the operation. Some time afterward, she also fell ill, and after her recovery, her discomfort, weakness and depression remained. After having become con-

scious of the conflict, which she had only partly confessed to herself, she found a new contact with her husband and became well again.

(*E*) As a fifth and last form, one finds the expansion of the hysterical psychism by the influence of extroverted feeling. Here the psychic influence can be still more disturbing than in the case of the feeling introvert, because the symptoms may destroy the relation with the surroundings. One finds pose, dishonesty and theatrical attitudes in a much more elaborate form than with primitive or extroverted persons, and if the contact with others is given up, pathologic states (dream states and fits of apathy) may be the result. Such cases tend to develop into long novels. This is a short abstract of one.

A woman, aged 45, separated from her husband for six years following some years of constant quarreling with him, lived with her little son and kept a boarding house. She was at odds with her family, with the maids, with everybody; at times she was destructive of property and tried to kill herself. At the same time, she succeeded in gaining the sympathy and confidence of people in her environment. Her life history was one long series of wrongs. A twin brother died shortly after birth, and, since he was the only son, her father always scolded her and said that she ought to have died instead. She had been scrofulous as a child and generally despised by everybody. At boarding school she developed well, and when she returned home, her father became interested in her sexually. She resisted, and he began to make things difficult for her, making her act as a servant, and submitting her to other indignities. Her mother did not dare to oppose him. When she succeeded in getting away from home, she met the same fate of being abused again and again. Often she worked for some time with great ability and success, doing nearly impossible things by sincere application to her work, but then some personal relation would touch her old complex. Then she exhibited astonishing talent in reconstructing the same kind of situations of her youth again, committing sexual offenses or letting herself be cheated or victimized in other ways. This resulted in a variety of hysterical symptoms: scenes, apathy, dream states, delirium conversions, etc. She became degenerated and had to live on charity, which she knew well how to solicit.

SUMMARY

I have tried to show that the group of disorders termed hysterical may be subdivided psychologically into smaller groups. In all of them, both certain preexistent tendencies (psychologic types) and certain acquired psychic mechanisms (psychisms) may play a rôle, sometimes one predominating, sometimes the other. Hysterical symptoms may arise in persons of any type when external circumstances become extremely difficult. They may be elicited with less provocation in the case of primitive or adolescent persons. In people of the extroverted types and in those whose predominating function is feeling, hysterical manifestations tend to develop more lasting and elaborate forms than in people of other types. These several groups are fairly distinct from one another in their manifestations.

It seems to me that this insight into different structures of hysteria may be useful, not only in understanding patients, but also in psychotherapy. When the psychism is most important, an analysis of it is necessary. If the general background of the character is of chief influence, then education in compensating the onesidedness is an important factor in therapy also.

DISCUSSION

DR. KARL BOWMAN: The distinction given between the hysterical personality and the hysterical reaction is in line with the tendency in schizophrenia, in which there is the concept of the schizoid personality and the schizophrenic reaction. Dr. van der Hoop has discussed the way in which the different schools have approached the problem of hysteria, mentioning particularly the German School, the French School and the psychoanalytic School. I would point out that there has been a common tendency to emphasize the constitutional factor in hysteria. Freud has continually admitted the importance of the constitutional make-up, but most of us have been so interested in Freud's discussion of mechanisms that we have lost sight of the fact that he goes back to the constitutional factor as the final explanation. In Freud's recent book, "The Ego and the Id," he emphasizes the great importance of the method by which a person deals with the Oedipus complex, and says that one's later development is dependent on this fact. He then states that the way one deals with the Oedipus complex is dependent on the constitutional make-up. Dr. van der Hoop has recalled Jung's classification of the introvert and extrovert. There are many classifications of personality and different people prefer different classifications. It is not a question of absolute validity of one concept as opposed to another. Such concepts of personality are merely tools with which one works, and by means of which one tries to understand patients. To some persons the concept of introvert and extrovert is a satisfactory tool. To me there is no greater advantage in this concept as opposed to various other concepts, such as those of Kretschmer, Bleuler and various other writers. Perhaps this is because I am less familiar with the concept of introvert and extrovert. Dr. van der Hoop has been working with it for many years; he has developed these subtypes which he has explained in a slightly different manner from Jung, and has given his experience in using these concepts. We have all appreciated hearing his discussion of the subject, and should now inquire whether we can make use of these tools which he has shown us in working with our own cases. This is the practical test of any theory. Dr. van der Hoop has tried out the method and thinks that he gets good results with it.

DR. DONALD GREGG: Do you make a distinction between introversion and introverted feeling? and between extroversion and extroverted feeling? It is not clear to me whether or not you subdivide introvert persons into those with introverted feelings and extroverted feelings, and extrovert persons into those with introverted feelings and those with extroverted feelings.

DR. VAN DER HOOP: All these classifications must be used as tools; to this I agree. The classification which I am advocating has become very useful to me. In my mind, the more familiar distinction between introversion and extroversion seems less important than the differentiation of the four functions, instinct, intuition, thinking and feeling. Each has its importance in psychiatry, but in hysteria the function of feeling is most important, so in this paper I have confined my attention to that.

AFFECTIVE REINTEGRATION IN THE SCHIZOPHRENIAS *

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HISTORICAL REVIEW

The consideration of psychoses in proper perspective can be made only if one bears in mind that less than a century and a half ago it was thought legitimate in some quarters to debate the question whether or not severe mental illnesses belonged to the domain of medicine. True, the medical profession always strove with greater or lesser success to find in medicine a proper place for psychopathology, but one must not lose sight of the fact that only 130 years ago the philosopher Immanuel Kant, in response to the physician Hufeland's psychiatric contentions, insisted that the consideration and treatment of mental diseases belonged rightly to the philosopher and not to the medical man. Nor was psychology considered a sufficiently respectable discipline until about 110 years ago, when August Comte reserved for it a special place in his classification of sciences. Mental diseases, particularly those psychoses which are today covered by the concept schizophrenia, were considered disturbances of the mind in the narrow sense of the word, i. e., the intellect and will. The rapid growth of knowledge of neuro-anatomy stimulated the greatest number of investigators in the direction of cerebral localization, so that from the beginning of the nineteenth century the neurologic or somatologic schools began to dominate the field of psychiatry; Georget, Esquirol and Broussais, in France, and Friedreich and his generation in Germany were the first representatives of this manner of viewing psychoses. On the other hand, the rapid strides made by experimental, physiologic psychology toward the end of the last quarter of the nineteenth century offered a number of new data with regard to the intellectual processes of man—which were soon utilized by clinical psychopathologists. The various purely psychologic theories of mental diseases were gradually pushed into the background; they all lacked proper empiric foundation and were still too closely related to metaphysics; thus the endeavors of Stahl or Heinroth, and in the middle of the past century of the almost forgotten Carus, assumed an insignificant, if any, rôle in the consideration of those diseases which today are called schizophrenias. A severe and apparently chronic mental disorder was considered primarily

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a disorder of the process of thinking, of mentation, of cerebration. The primacy of the cognitive formations of personality was thus recognized as an indisputable principle and fact. This was in a general way the orientation which reigned in the field of psychiatry toward the close of the past century.

If one now casts a glance at the past thirty-five years, one will be impressed by the extraordinary energy with which the study of chronic psychoses has progressed. As a matter of fact, the last thirty-five years brought to light more instructive facts and produced more useful working hypotheses with regard to so-called chronic psychoses than the 400 years which elapsed from the time when Magnus Hundt made use for the first time of the word "Anthropologia" in his "Nature of Man" (1501), or since Juan Luis Vives first gave an empiric study of affects as the primary source of mental disorders (in his "de Anima et Vita" published in 1538).

One can hardly speak of, and therefore would search in vain for, any really rational therapy for severe psychoses at the end of the nineteenth century. Two fundamental things were lacking without which no therapy was possible: a systematic nosology and a working hypothesis as to what the nature of the psychosis was. It is as interesting as it is significant that toward the close of the past century the first and most serious and most successful attempt was made to fill in both these gaps; in 1896, Kraepelin established the nosologic entity of dementia praecox, and in 1894, Freud published an article on "The Defence Neuro-Psychoses"; in 1900, his "Interpretation of Dreams" appeared, and in 1901 his "Psychopathology of Every Day Life"—thus uncovering a new field of empiric psychologic data which gradually led to a deeper understanding of psychodynamics.

It must be emphasized again that without at least a cursory historical reconstruction like this one of the whole development of one's views, it would be hard to understand and still harder to apply present day working hypotheses to the therapy of schizophrenia.

Kraepelin, true to tradition, was interested in how the patient thought; he frankly admitted that the specific ideas, what we call today the mental trend, were of no significance; he followed the old path of the formal associativistic psychology of Wundt and was interested in the formal mechanics of pathologic thinking which he observed in his schizophrenic patients. As one cannot reason with irrational people, any therapy of a psychologic nature was naturally out of question. Moreover, the kraepelinian principle of basing the diagnosis on the principle of poor prognosis or occasional rare and temporary spontaneous recovery tinted his whole system with a fatalism which discouraged any active thinking along the lines of possible effective therapy.

However, the kraepelinian orientation, despite its persistence in many psychiatric quarters even today, was abandoned extremely soon. About ten years after Kraepelin's nosologic outline of dementia praecox, paranoia and paraphrenia, a newer and broader psychobiologic orientation made itself felt. Adolf Meyer (1906), Carl Jung (1906) and the earlier psychoanalytic workers (Freud, Bjerre and Maeder, between 1894 and 1910) showed a definite and decisive deflection from the fundamental implications of kraepelinian phenomenologic formalism. Yet these deflections were unable to mitigate at once and appreciably the helplessness with which the psychiatrist had to face the schizophrenic subject. It took more than another five years, and a new momentous turn was made by the contribution of the Zürich group headed by Bleuler. It is not an accident that the newly coined term schizophrenia at once became universally accepted and at once replaced Kraepelin's dementia praecox. The history of clinical psychopathology knows innumerable attempts to coin new words; their popularity, however, could be measured in inverse ratio to their numerical growth. The secret of Bleuler's success lies in the new and aggressively creative turn made by clinical psychiatry. The whole structure of Bleuler's concept is of such a nature that it opened new perspectives for the therapy of a condition which heretofore was considered hopeless, as a matter of course. Bleuler preserved only some of the minor and purely external characteristics of Kraepelin's system. Thus the latter's subdivisions of dementia praecox are followed rather closely; too, Bleuler, like Kraepelin, saw in the intellectual disorder of the psychotic subject the factor of primary importance; he, like Kraepelin, remained influenced at least partially by the traditions of wundtian psychology.

On the other hand, the whole body of kraepelinian symptomatology is put by Bleuler into the class of secondary symptoms; in other words, what one became accustomed to call the formal picture of the psychosis was ascribed by Bleuler to a secondary elaboration of the primary disorder, which to him was the disturbance in the character of mental associations and the disturbance of affectivity.[1] These theoretical constructions of Bleuler were not merely the product of a brilliant speculation; they were the result of a systematization of an enormous empiric material, of actual and incontestable observations. The most important blow dealt by Bleuler to the kraepelinian system was the finding that schizophrenic subjects do not necessarily deteriorate, that the prognostic fatalism of Kraepelin was unjustified, and that the outcome of a schizophrenic psychosis may and usually does depend on the therapeutic effort made by the psychiatrist.

1. In a personal conversation Bleuler stated to me that he now considers these two disturbances essentially as one.

If one turns to the fundamental observations and concepts which, forming the foundation of Bleuler's views on schizophrenia, had the most far-reaching influence on the development of the therapy of schizophrenia, one will find the following: The prognostic criterion for diagnosis having been set aside as useless, the criterion of schizophrenia, i. e., of splitting of the personality as the most outstanding symptom, was introduced. The concept of autism was brought to the fore. The patient's personality appears split; the patient's psychic life is introverted; his affect is withdrawn from reality and expresses itself through autistic fantasies. It is not right, then, to say that the schizophrenic subject has no affect. The affective energies of the patient are frozen, so to speak, but not dead. Bleuler cited many instances of reawakening of the affective life of some of his patients who for many years appeared deteriorated and "affectless."

One thus comes to the central problem which concerns one when one faces a schizophrenic patient: What is the deeper nature of that process which appears to freeze, so to speak, the affective life of the patient, and what would be the best approach for the remobilization of the affective energies? In health the patient's affect is mobile and is shifted from one inner or outer object to the other as necessity demands; in other words, the personality is integrated to meet the various psychobiologic internal and external necessities. In schizophrenia one deals with a situation in which the withdrawal from reality is so great that the personality is deeply disintegrated; the affect is withdrawn from a considerable part of the ego functions. Any practical attempts to bring about a possible affective reintegration were thus unthinkable before Bleuler formulated and systematized his observations.

Yet Bleuler failed to work out any consistent method of systematic psychotherapy which would go deep enough into the analysis of the personality and thus produce that degree of affective reintegration that could lead the patient to real recovery. That is the reason why he had to introduce the concept of "social recovery" of schizophrenic subjects as differentiated from "medical recovery," which latter he considered of doubtful possibility. It may be remarked in passing that any methods, other than psychotherapeutic, i. e., physical and physiologic, are considered by Bleuler and his co-workers only as subsidiary and preparatory to psychotherapy; the Dauerschlaf method introduced by Kläsi was from the outset considered as a method for making the schizophrenic patient more accessible to psychologic treatment and not as a primary method of cure. The attempts of Kretschmer lead to the same results as those of Bleuler. Kretschmer, using a method of semipsychoanalytic approach, seldom attained more than a "social recovery" and introduced the term "façade psychoses." One should not underestimate, however, the value of these results, for after all, sur-

gical measures, particularly those for fractures, seldom succeed in bringing about a restitutio ad integrum. A certain amount of shortening of the leg or even an amputation of a limb is a deformity, to be sure, but it is accompanied by a cure of a dangerous condition which otherwise might have resulted in the death of the patient.

In psychiatry, however, such "recoveries with defect or deformity" are more dangerous than in surgery, because any recovery without the removal of the psychologic causes of the psychosis usually ends in a recurrence which carries in its wake more psychologic defects and more affective deformities. Statistical data, as yet, fail to convince one that a social recovery alone is a guarantee against recurrence or against a gradual continuation and further development of the schizophrenic process. The socially recovered patients, with rare exceptions, fail to establish a complete affective contact with reality. Mere intellectual insight and the ability of schizophrenic subjects to keep silent about the things which they know people consider pathologic is not sufficient to be considered a recovery.[2]

One could consider a recovery real only if a sufficient degree of affective rapport with reality and affective insight is reached; for even a neurotic person is unable to make a complete adjustment if his insight remains only intellectual; however, the vagueness with which Bleuler left us with regard to the real nature of the disturbances of associations, i. e., of the intellectual field, made it well nigh impossible and methodologically unjustifiable to attack the emotional life of the schizophrenic subject for purposes of therapeusis; as long as the queer thinking of the schizophrenic subject remained a riddle, it could not be influenced with any degree of system or even certainty.

Soon, new light was thrown on this problem too. One will recall that Bleuler's insight into schizophrenia was due mainly to his early utilization of the psychoanalytic point of view and therapeutic approach; he was one of the first practical psychiatrists who recognized the validity and the importance of the freudian observations on infantile sexuality and on the unconscious nature of psychologic conflicts, some constellations of which were known in those days under the name of complexes, i. e., constellations charged with a great deal of affect. As has been said, Bleuler, while endeavoring to understand the language of the schizophrenic subject, dealt with schizophrenic thinking in a formal way. That the peculiarities of this thinking are of a deep affective etiology he undoubtedly sensed, but the ethnologic contributions of Freud were at that time yet to be made, and Bleuler's observations, correct in substance, remained to be explained.

2. Bleuler and his co-workers rightly consider the so-called insight (intellectual) as of little importance.

These ethnologic studies, in which Freud attempted to compare our psychic life with that of primitive races, opened a new field of investigation and new vistas for psychopathology. No contribution in recent years enriched the understanding of psychoses more than the introduction of ethnology into psychiatry. Soon it became increasingly clearer not only that some of the seemingly inborn conventions of the civilized race represent a reverberation of primitive customs, but that neurotic subjects not infrequently represent a symptom-complex which is but a regressive expression of various and long forgotten superstitions and habits of the primitive man. These views served as an impulse for a number of restudies in the field of ethnology, and the past ten years witnessed the appearance of a number of investigations which threw a new light on the nature of primitive thought and on the singular similarity which can be observed between primitive and schizophrenic thinking. Not only could such contributions as those of Levy Brühl be profitably utilized for the demonstration of such similarity, but the whole technic of the language of dreams became clearer in the light of ethnologic explanations. The work of Niewenhuis, the wealth of material offered by Frazer, the general studies in genetic psychology and history of religion began to be utilized by psychiatrists for the comparative studies of schizophrenic persons, and it might be considered an established fact that schizophrenic thinking is a highly complicated process which has its own logic and which hardly differs from the pattern of primitive thinking. In other words, that primary disturbances of associations, to which Bleuler called attention, represent apparently nothing else than a regression to a pattern which appeared to be lost by modern man, but which is apparently preserved in the unconscious. The child in the early stages of development takes recourse to the same mode of thinking, so that the adult today carries within him both the philogenetic and the ontogenetic roots of that mode of thinking in magic symbols and apparently disjointed projections which are so characteristic of the schizophrenic subject.

For my purpose it is unnecessary to go into the details of schizophrenic thinking. For these the reader is referred to the contributions of Freud, Jung, Schilder, Reik and Storch. Suffice it to say that comparative clinical and ethonologic studies leave at present no doubt that "schizophrenic thinking is not rational thinking, but rather a process carried along by an emotional undercurrent" (Storch); in other words, the most outstanding disturbance found in schizophrenia, that of mentation, became, as a result of deeper studies, reduced to a disturbance of emotional nature. To continue with Storch: "these irrational units of affective experiences and thoughts are only imperfectly accessible to

rational analysis. Such analysis can only be undertaken by way of emotional participation and sympathetic understanding and these latter will always be the most valuable means for penetrating the world of thought of the schizophrenic."

PERSONAL OBSERVATIONS

As a result of the development of views on the psychology of schizophrenia that have been sketched, the methods of investigation and therapeutic approach changed considerably. One might repeat the able statement of McCurdy and say: Whereas the Kraepelin psychiatrist was interested in how the patient thinks, the psychiatrist of today sees in what the patient thinks a clue to the understanding of the inner conflicts and indeed of the whole structure of a given schizophrenic psychosis. Purely statistical studies of a large number of cases, which enabled one hitherto to construct a sort of a composite picture of schizophrenia, no matter how important and illuminating, discount the purely individual by their very nature. Such studies naturally tend to establish a sort of a common denominator. Yet it is only the intimately individual, the characteristically personal, history of the psychosis, its outer as well as its inner history, that helps one to obtain some light on its genesis and development. As to the method of obtaining such a history, it is a well known fact that the question and answer method of studying a patient reflects not infrequently the personal bias of the physician, and as it colors the results of the investigation by the theoretical preconceptions of the investigator, it fails to yield satisfactory scientifically correct results.

These considerations led us, in Bloomingdale Hospital, to attempt a psychoanalytic study of schizophrenia. The psychoanalytic method, as is known, requires a strictly passive attitude on the part of the investigator, interpretations and explanations being given to the patient only when the patient is affectively ready, i. e., when the patient through the accumulation or display of the affect which is related to this or that trend is about ready to gain insight almost entirely without explanations or interpretations; this method, if properly applied, thus excludes any intellectualization—the chief enemy of insight, and in schizophrenia the most dangerous enemy, because the schizophrenic person is an intellectualist *par excellence;* he could, would and does indulge in most complex intellectual formulations in order to avoid the necessity of emotional participation in reality. Another advantage derived from the psychoanalytic method is that if a patient is permitted to talk and "ramble along" freely without interference, he sooner or later, but quite invariably, stumbles on "resistances," i. e., on psychologic elements which are charged with a great deal of affect, and it is possible to observe clearly and even to estimate the depth of the affect long

before it comes to full expression. The patient's voice, minor and major gesticulations, facies, sudden silences, evasions, etc., all serve as excellent indicators and signs of warning.

One case will be reported briefly. Again, it should be borne in mind that while the larger the number of cases the more instructive the observations, a longitudinal study of even one case reveals much more than a cross-section study of a great number. This case history, made up of detailed records of about 450 interviews of one hour each, represents a bulky record of 2,000 pages [3] and only those parts of it which pertain to the problem under discussion will be reviewed briefly.

No attempt will be made to enter into the details of the technic. The discussion of various psychologic reconstructions and finer metapsychologic data will also be omitted, for it might serve only to obscure the main issue.

REPORT OF CASE

A woman, aged 34, when admitted to Bloomingdale Hospital, was oriented as to place, time and person. She had auditory hallucinations. She said that her whole body was changed, that she was pregnant; that she was receiving messages from various people; she saw many mysterious meanings in things, expressed antagonism against her family, and appeared preoccupied and "far away." Her behavior changed rapidly several times a day; from a state of comparative composure and calm, she would suddenly enter into a semiconfusional state, when she would scream, sing, "undergo operations," move her body in a rhythmic, erotic manner and then quiet down and remain motionless as if in a stupor. A few months after admission, she quieted down to such an extent that objectively she appeared a normal, pleasant, somewhat dreamy person without many signs of asocial behavior.

There was no physical illness or defect coloring her mental state. She was an excellent sportswoman, and played tennis and golf well; she excelled in the arts and crafts which she learned in the hospital.

To her physician she admitted that she "might have been sick," but this, as it was learned later, was more in the nature of a forced admission than a real conviction, for underneath she continued to harbor the old ideas of reference with which she lived more or less for almost four years before she was hospitalized and which reached the phase of an acute episode at the time of her admission. Some one was in love with her. He communicated with her by means of "signs." These signs she read in the ink spot on the blotter of her desk at her place of work; later, in newspapers: in an advertisement, in a report of an accident or in the social news column; her work was directed mysteriously by "them" from the outside. Without paying attention to what she was doing, in fact without being interested, she would succeed in doing it excellently (subjective impression) because she was "guided by them." She saw beautiful lights; she went through various fantastic experiences and erotic perversions "in spirit, yet in fact." She fantasied various tortures, such as men whom she had known tied to trees or poles, their penises tied to one another; the poles or trees would

3. It is hoped that it will be possible later on to publish this case record fully in monograph form.

be felled in opposite directions so that the penises would be torn out of the men. When a billiard ball was accidentally left on the billiard table of the hospital hall it was a message to her, the nature of which depended on the color of the ball.

She understood "all the hints" which she overheard in the conversations of others. In short, she represented a typical case of paranoid schizophrenia with a pretty well systematized set of delusions. She was to be married. The man in question, although married and having a child, was making fantastic preparations to marry her, but he was doing all this secretly; she would not explain why; she was not interested in explanations; to her, her delusions were facts; her mood (no perceptible swings) depended on the various messages she was getting. Before she came to the hospital, as well as during her stay there, various numbers had special meanings. Two meant "good," three was "yes," five meant "no" and "bad." For a time her actions depended entirely on these numbers. Two steps, two shouts, two strokes of the clock; five bells in the distance (actual or imaginary) made her go on with or stop what she was doing.

She learned to control her outward behavior. She appeared quiet, composed, friendly, dreamy—with an obvious bent to forming friendships in which she was greatly admired but to which she would contribute nothing except a certain queenly poise and gentle dignity. Only later, toward the end of her first year in the hospital, did she become affectionate (reservedly) and obviously erotic with another older woman patient, but apparently without being aware of it.

Her family history was not complicated. The paternal grandmother died at 87, suffering from what appears to have been a senile psychosis; her mother died at 55, when the patient was 21, of carcinoma of the uterus. The patient was the third of six children. None of the siblings showed any psychopathies, except an older sister who was a somewhat too ardent Christian scientist, but rather well adjusted socially. She had always been egocentric and shut-in.

Analysis began one year after admission, and continued regularly for about ten months. An interruption of twelve months followed, during which the patient lived outside the hospital, well adjusted, satisfied, inwardly very sensitive and responsive to attentions of men, especially older ones, but outwardly showing none of her real feelings. Her paranoid trends disappeared totally before she left the hospital; during the following year, she was free from delusions and hallucinations; nor did she show any tendency to gravitate toward ideas of reference; she was free from suspicions, but rather insecure, and eager to complete her analysis, which was interrupted because of the unavoidable absence of her physician. She resumed the analysis, but continued to live outside the hospital and work steadily, free from signs or symptoms of mental illness.

As has been said, the wealth of material obtained from the patient does not permit reporting it fully. Many details must be omitted.

The following was disclosed in the analysis: She had an apparently acute episode, which appeared like a confusional state and which developed in a period of several days as a result of a fantasy that she was going to be married to the man whom she saw daily and who "was in love" with her without showing any objective sign of it, but who was supposed to give her secret signs of love and of his plans. This fantasy developed crescendo after it became known that a child was born to him (he actually married about one year previously—the patient knew about it). This episode, which brought her to the hospital, was not the beginning of the illness. She had been insecure, "shaky" and worried that something was wrong with her body, her genitalia, etc., for about ten years. Her ideas of reference, her tendency to elaborate everything into a fantasy began ten years previously, when a young man, who was engaged to her, once while making

love to her remarked "You behave as if you loved before." She then bluntly confessed that she once masturbated a friend of the family who was much older. The young man, furious, broke off the relationship. Actually the patient was an innocent virgin. She knew little if anything about sex despite her age of 24; yet she had a rather eventful love history.

At the age of 10, an old friend of the family and a highly respected gentleman, masturbated her. In her teens she was attached to a Sunday school leader who was successful in teaching boys and girls how to avoid temptation. He was very popular as a leader in moral behavior. He made love to her, kissed her and once said that if his wife died, he would marry the patient. He was about 60. The patient at that time was 18. In her twenties she went through the happiest period of her life, taking care of her father's household after the death of her mother. She then observed (stealthily) that her father masturbated and that her brothers masturbated. Singularly enough, she observed these things, was aware of them and of their sinfulness, but yet did not quite see clearly the sexual implications. She did not know how the sexual act was performed. She masturbated in her childhood—from the age of 4—then stopped, but resumed after her father remarried. When 5 years of age, she saw the penis of her baby brother and wanted to tear it off. At about the same age, she saw a man exposed and masturbating in front of a window and was extremely frightened.

Her father once cruelly beat their dog with a stick. She once masturbated that dog (she must have been about 8 then). She recalled also that, when about 8, she once sat on the floor tying a shoestring for her mother; the mother was getting dressed, and the girl discovered the existence of pubic hair for the first time and was frightened.

From about the age of 19, men began to pay a great deal of attention to her. Almost automatically she would develop fantasies of love and marriage when reality little warranted such dreams. She would strike up relationships mostly with married men, and with two of them the affair went so far as her spontaneously masturbating them, she receiving no special pleasure from it. She appeared "somewhere far away." She never thought of intercourse, and when masturbating herself was not aware of any imagery.

From the whole mass of memories, impressions and events, the following picture was reconstructed (mostly by the patient herself): She "always" had (unconscious) fantasies of having a penis. She was a man. Under the apparent poetry of being in love lay hidden a great hatred for men. She wanted to deprive them of their members; masturbating them meant tearing their genitals away. She had early fleeting memories of having loved her mother—her breast—but then her whole unconscious life began to be dominated by hatred of mother and love for father. Some time very early in childhood, that love for father became hatred because of the father's preference for mother and the older sister. From that time on she loved only herself. Once under analysis she actually recovered a fantasy of being a man and loving herself as a woman, having intercourse with herself. Unconsciously she never wanted to marry and had severe homosexual drives which disappeared under analysis and became transformed into the normal heterosexual drive; this, however, she did not reach before she recovered emotionally and in memories her feminine, passive attraction to her father.

At this point it should be emphasized again that the case report is made deliberately sketchy, for what is of interest at present is the therapeutic result and the affective behavior of the patient which will be discussed presently.

The patient had always been a deeply religious Episcopalian (High Church). She was imbued with sermons and a strict sense of propriety. She was strictly

chaste; even at 34 she did not know the mechanics of sexual intercourse (unconsciously she did, but she did not permit herself to know it consciously). Possessed of an extremely noble sense of duty and propriety, she was dominated by an almost cruel conscience. She never used or knew "bad words," even at 34. (Again it was disclosed that she knew them unconsciously.) She was at times "almost tortured" by a minor break of social etiquette.

During the first six months of the analysis, the patient's behavior was typical of a schizophrenic person. She spoke clearly, evenly, related her trends, ideas and delusions without apparent emotion or even tension. The even bluntness of her affective attitude was so conspicuous that at times it seemed that the analysis would have to be given up as a failure. Gradually, however, the whole structure of delusion dwindled away. During these months her dreams and some of her memories were clearly indicative of infantile conflicts, but the analyst deliberately left them aside for future reference. The whole analysis was concentrated on the differentiation between reality and fantasy, past and present. Almost no attention was paid to transference situations. It is only after this period of analysis of "the reality principle" was completed that the deeper analytic material was approached.

Proceeding much more slowly than a neurotic person under analysis, the patient gradually began to approach several situations which were charged with a great deal of affect, but, characteristically enough, instead of discharging the affect she began to day-dream of the future, or to speak of her great affection for the analyst; this period of the analysis, while yielding a great deal of information and of unconscious material, failed, however, to bring out the affect in its full value; yet all symptoms disappeared, and one could at that time state confidently that the patient recovered socially *in toto*, that her affective recovery was slight, and that her affective insight was almost untouched. It was at that time that she left the hospital, to return to the analysis one year later.

As has been said, she was well throughout the year, but she failed apparently to establish any real object relationship. The transparent rationalization was: "I must wait until the analysis is over and then." . . . Actually she shunned any contact with real life.

The analysis resumed, she related that she was in love. She was ready to establish a love relationship, but did not dare. One day she stated that she had decided to give herself to the man she loved. This was the turning point of the analysis as far as her hidden affective life was concerned. She developed rather suddenly the fantasy that the analyst was trying to prevent the relationship "for her own good." He was a detective. She knew it was not true, but could not prevent the intrusion of that thought. In a period of two weeks she actually repeated her whole psychosis: ideas of reference and ideas of persecution, and a whole system of elaborate delusions, old and new ones, cropped up in the form of obsessive thoughts. The patient relived in the analytic setting the whole pattern of her delusional system, discharging at the same time a great deal of emotion. She repeated and moved through a mass of memories and infantile fantasies—all traumatic incidents of a sexual nature—and came out of this analytic period in a state "very peculiar to me." She saw "people and the streets in a different light, as if I can touch them; before, there was a veil, or a mist."

The whole demeanor of the patient throughout that period was that of a person of great and deep emotions which overwhelmed her. She began to show a definite contact with reality which coincided with a new awareness that she "loved the world and people." She began to meet people with ease and pleasure.

COMMENT

It seems that the crucial and most fundamental element of the whole analysis was the patient's reliving and reacting her paranoid psychosis in a stormy way in a period of about two weeks in the analytic situation. While the characteristics of this situation are that the analyst is utilized as a sort of a screen on whom the conflict is projected, the sense of reality is actually never lost. The patient is caught in a sort of an emotional trap. The psychotic elaboration of the conflict is lived through on the analyst, while the awareness of the reality situation prevents any escape into the former psychosis, and the tension resulting therefrom brings forth the emotional discharge. It is a struggle for a permanent recognition of reality; in other words, the process with which the analyst began is continued and repeated in a setting full of conflict.

Such a situation would have been impossible if the earlier phases of the analysis were not devoted to the care of "the reality principle" rather than of the analytic situation; the analytic situation being the one usually attacked first, it would appear that the lack of success with which analyses of schizophrenic subjects have so far met, ceteris paribus, was due mainly to the failure to realize the importance of this technical consideration.

In other words, the analysis of schizophrenic persons requires a preliminary period of "reality testing" which the patient, strange as it may seem, does himself.

I must emphasize that the considerations outlined here are of tentative and preliminary nature. No claim for the cure of schizophrenia is here made. That the patient reached an unusual level of normality is incontestable, but one must, of course, be aware of the fact that only further sustained experimenting will throw further light on the matter.

Moreover, it is doubtful whether any type other than the paranoid is amenable to analysis.

Since the report of Bjerre who, in 1910, claimed to have cured a woman, aged 53, of paranoid schizophrenia, many reports have appeared in psychoanalytic literature, but they were mostly of theoretical nature (Nurnberg, Tausk, Wälder).

One fact, however, appears beyond doubt. The analytic procedure in its classic form—preceded by a preliminary and rather long period of analysis of the "reality principle"— mobilizes the masses of affective energies which otherwise remain shut in and prevent a proper contact with reality.

The significance of this cannot be overlooked. It throws a somewhat different light on the phenomenon of "Schizoidie." It is not

impossible that what one calls schizoid personality is actually not an established constitutional form, but a complete resultant, a derivative of certain dispositions only. Under circumstances of great stress, such as a repressive, unusually strict parental ideal combined with early traumatic stimulations of sexual life, a conflict ensues which favors the withdrawal of the affect from active contact with reality and thus the overemphasis of the schizoid disposition.

The affect can be mobilized and set to expression. If the mobilization takes place after reality and fantasy have been differentiated by the patient, the process of affective reintegration may go to completion.

BARRIER BETWEEN THE BLOOD AND CEREBROSPINAL FLUID

III. DISTRIBUTION RATIO OF BROMIDES IN SCHIZOPHRENIAS*

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Within the last few years the investigation of the passage of substances from the blood into the cerebrospinal fluid and the ratio of distribution of these in the two fluids has attracted a great deal of attention. In the psychiatric literature this increase in interest has undoubtedly been due largely to the discovery of the occurrence of consistent characteristic changes in this ratio in schizophrenia. This discovery has been made possible by the development of a new method of procedure that was devised by Walter. The methods hitherto used, although different in many respects, had two main difficulties to contend with: 1. Some of the methods (the hemolysin test of Weil and Kafka, and the trypan blue and kongo red methods of L. Stern) were based on the demonstration of substances which entered the spinal fluid in certain pathologic cases only. Naturally, this excluded all possibility of discovering instances in which there was a decreased passage of substances into the cerebrospinal fluid. 2. Other methods (such as uranin, etc.) were dependent on the amount of a certain substance that passed into the fluid in a given length of time. But as the blood possesses many possible outlets of a variable nature, it was impossible to determine the actual ratio of the amount in the cerebrospinal fluid as compared to that in the blood at any given moment. In 1924, Walter[1] described a method which was successful in overcoming both of these difficulties.

Briefly,[2] it consists in the administration by mouth of 0.01 Gm. of an aqueous solution of sodium bromide per pound of body weight, three times a day for five

* Submitted for publication, Feb. 14, 1930.
* Read at a Meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 27, 1929.

1. Walter, F. K.: Studien ueber die Permeabilität der Meningen, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:522, 1925.

2. The procedure was reported in detail in the first communication: Malamud, W.; Fuchs, D. M., and Malamud, N.: Barrier Between the Blood and the Cerebrospinal Fluid: I. Changes in Permeability in Mental Diseases, Arch. Neurol. & Psychiat. **20**:780 (Oct.) 1928.

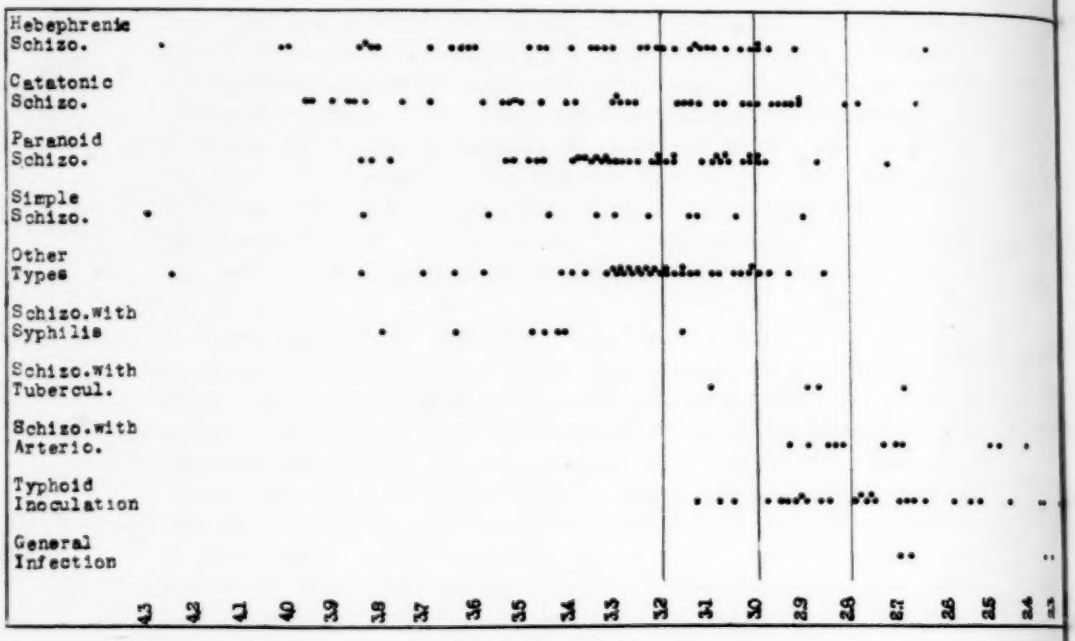
days. On the sixth day, cerebrospinal fluid and blood are removed simultaneously. The proteins are precipitated and filtered, and gold chloride is added to the filtrates of both blood and cerebrospinal fluid. This causes the formation of a colored compound, gold bromide. The fluids are then compared with each other in a colorimeter and also with freshly prepared solutions of bromide of known bromide content. By dividing the blood content by that of the cerebrospinal fluid, a distribution ratio (or quotient) is obtained. In normal persons the blood contains about three times as much bromide as is found in the cerebrospinal fluid, so that here the ratio is said to be 3 with fluctuations from 2.8 to 3.2.

This test, used for the investigation of the passage of substances from the blood into the cerebrospinal fluid, has most frequently been referred to as a permeability test or, by some authors, as a meningeal permeability test, the quotient obtained being spoken of as the permeability quotient. We believe that, so far, no conclusive evidence has been advanced to justify the assumption that a simple permeability mechanism governs the exchange of substances between the blood and cerebrospinal fluid. For this reason it was suggested in the first communication [1] that the term blood-cerebrospinal fluid barrier should replace that of permeability. For this reason also we shall report our results in terms of the distribution ratio of bromides rather than that of permeability.

By this method it is possible to demonstrate very minute quantities of bromide, and as some bromide always passes into the cerebrospinal fluid, one is able to study the decreases in the quantity as well as the increases. Furthermore, as the blood and cerebrospinal fluid can be examined simultaneously and compared with the standards, a true ratio of the distribution, after equilibrium is established, can be obtained. In this way, both of the aforementioned difficulties were successfully overcome. The first result of the utilization of this method was the discovery that in persons suffering from certain diseases there is a decrease in the amount of bromides that pass into the cerebrospinal fluid as compared with that of normal persons. Of the different diseases encountered in hospitals for mental and nervous diseases, the schizophrenias showed such decreases in a most pronounced fashion.

In the first communication on this subject, it was possible to corroborate most of Walter's statements in principle. It was found that the method was reliable in that the distribution ratio in cases in which the disease process did not show changes remained the same on repetition; the change in the color of the fluids tested was really due to the bromide content and not to some other chemical changes; also definite and consistent deviations from the normal were found in certain diseases of the nervous system. In that communication we reported the results of investigations of the bromide distribution in a large number of cases representative of the different diseases usually encountered in a state hospital population. Depending on the bromide distribution

ratios, these diseases seemed to fall into three definite groups: 1. Practically all patients suffering from mood disorders, senile psychoses (uncomplicated by arteriosclerosis), psychoneuroses, chronic alcoholism and involutional melancholia, fell within the limits of from 2.8 to 3.2, which we also considered as the limits of fluctuations in normal persons. 2. In all patients suffering from definite organic disease of the central nervous system, and especially when the capillary network and arterioles of the cortex were affected (dementia paralytica, cerebral arteriosclerosis, etc.), the distribution ratios were below 2.8; i.e., the



Distribution ratio in schizophrenia.

amount of bromides that passed into the cerebrospinal fluid was increased as compared with the normal. 3. A number of diseases, which consisted mainly of the different types of schizophrenia, fell into a group by themselves, characterized by distribution ratios that were either within the normal limits or above 3.2, i.e., in which there was a lessened passage of bromides into the cerebrospinal fluid. Since the publication of the first communication, we have continued to work on the distribution of bromides and are now in a position to report on a larger group of schizophrenias in which these ratios were determined.

In the chart we have tabulated the distribution ratio determinations in 210 cases of schizophrenia (this includes 95 cases reported in the previous communication). The black dots represent separate deter-

minations. The figures at the top and below the chart denote the distribution ratios beginning with 2.2 and going up to 4.3, with the midline at 3 for normal. On the left side of the chart we have indicated the different types of schizophrenias with which we were dealing. The first five groups represent the usual classification of schizophrenias into hebephrenia, catatonia, paranoid, simple and other types, all cases reported in these five groups being apparently free from complications by any somatic disease. As can be seen in the chart, all but four of the ratios in these cases fall above (that is, to the left) the line at 2.8, and most of them are above 3. As regards different types of schizophrenia, we did not find any very definite correlation of the ratios with the types, although there seems to be a slight predominance of high ratios in the hebephrenic type, decreasing gradually as one descends through the catatonic, paranoid, simple and other types.

Below the five main groups we have tabulated the cases of schizophrenia that were complicated by some somatic diseases. In a group of patients with schizophrenia with a positive Wassermann reaction of the blood, but with no serologic or neurologic signs of syphilis of the central nervous system, the ratios resembled those in uncomplicated cases of schizophrenia. The groups tabulated below this one, however, show a different picture. Thus, for instance, the patients with schizophrenia having active tuberculosis, acute infections or cerebral arteriosclerosis almost always show a definite lowering of the ratio, most of them being below 2.8. In some of these cases we were able to prove in a striking fashion that the low distribution ratio was actually due to the physical condition. One patient with dementia praecox, paranoid type, was found to have a distribution ratio of 3.35 on admission. During her stay in the hospital she developed a rather acute pulmonary tuberculosis, at first with a subfebrile temperature; later, it became higher. Shortly after the first signs of infection were apparent, a bromide test was made and the distribution ratio was found to have fallen to 3.08. Two months later, when the signs of tuberculosis were much more severe, another determination revealed the distribution ratio of 2.68. The patient died, but it was not possible to study the condition of the vessels in the brain to see whether definite changes in these could be found. Serologic examinations showed no signs of meningeal involvement, however. This corroborates the statement of Stern [3] who found an increase in the passage of substances from the blood into the cerebrospinal fluid in animals inoculated with tubercle bacilli.

A still more striking example of the influence of physical diseases on the distribution ratio in schizophrenia was afforded by determinations

3. Stern, L.: La barrière hémato-encéphalique, Schweiz. Arch. f. Neurol. u. Psychiat. **8**:604, 1923.

made in patients during the period when they were receiving injections of typhoid vaccine. Here we were able to demonstrate in a large proportion of cases that the vaccine caused a definite lowering of the ratio. As is seen in the chart, in the group marked typhoid inoculations all the distribution ratios are below 3.2 and most of them fall below 2.8. In order to determine the actual relationship between the typhoid inoculation and the distribution ratio, we repeated the determinations in these cases some months after the inoculation was given, and the results are shown in table 1.

The facts brought out in table 1 are important when one considers the controversies that are taking place now between different observers in this field. Even in our first contribution we were able to show that in a certain number of schizophrenias the low ratios could be explained

TABLE 1.—*Influence of Typhoid Inoculation on Distribution Ratio*

Name	Diagnosis	First Determination	Second Determination
R. H.	Schizophrenia, other types	283 (1/12/28)	384 (11/29/29)
J. C.	Schizophrenia, paranoid	313 (3/ 8/28)	384 (12/12/29)
J. H.	Schizophrenia, hebephrenic	291 (4/16/28)	346 (12/ 5/29)
M. W.	Schizophrenia, hebephrenic	275 (1/16/28)	345 (12/ 5/29)
L. P.	Schizophrenia, paranoid	286 (1/19/28)	333 (7/12/28)
G. W.	Schizophrenia, other types	257 (9/ 6/29)	324 (11/29/29)
J. P.	Schizophrenia, catatonic	268 (3/14/29)	315 (12/12/29)
J. D.	Schizophrenia, other types	197 (5/17/28)	313 (11/ 1/28)
G. J.	Schizophrenia, catatonic	277 (8/ 2/28)	306 (12/ 5/29)
G. S.	Schizophrenia, other types	270 (9/12/29)	304 (11/29/29)
J. S.	Schizophrenia, catatonic	294 (6/ 2/27)	301 (12/29/27)
R. L.	Schizophrenia, other types	276 (2/ 9/28)	300 (12/ 5/29)
C. M.	Schizophrenia, hebephrenic	264 (10/ 4/28)	292 (12/ 5/29)
G. V.	Schizophrenia, other types	303 (6/21/28)	300 (12/12/29)
J. C.	Schizophrenia, other types	309 (8/ 7/28)	300 (12/ 5/29)
M. B.	Schizophrenia, hebephrenic	264 (4/19/27)	259 (12/ 5/29)
E. D.	Catatonia (? toxic)	276 (8/16/28)	263 (11/22/29)

on the basis of some organic disease that was present at the time of examination. We pointed out at that time (and this was recently emphasized by von Rohden [4] and others) that, in carrying out the bromide test, great care is necessary to avoid such sources of error. If the investigations of the distribution ratio of bromides in schizophrenia are to have any value at all, it would seem essential to avoid all known sources of error. Of course, we do not mean that we are entitled to assume that all low quotients are due to known or unknown sources of error. Nevertheless, we believe it important that every case should be studied individually for factors that might influence the distribution ratio.

In analyzing the distribution ratios found in cases of schizophrenia that were apparently uncomplicated by physical disease, we find that a large group (60 per cent) show abnormally high figures. In other

4. Von Rohden: Ueber die Bedeutung der Permeabilität, Arch. f. Psychiat. **87**:797, 1929.

words, in these cases there is a decrease in the passage of the sodium bromide from the blood into the spinal fluid. In 2 per cent of the cases the distribution was below 2.8, leaving 38 per cent with determinations that fall within normal limits. As already stated, there is no apparent parallelism between the ratios and the different types of schizophrenia as it is usually classified. When one considers how indefinite the lines of demarcation between these different groups can sometimes be and how arbitrary the classification often becomes, one

TABLE 2.—*Distribution Ratios in Twenty-Seven Cases of Schizophrenia*

	Out of Hospital	Distribution Ratio	
(a) Patients Dismissed from the Hospital Showing Good Remissions			
1. C. A.	6 months	1.84	(typhoid inoculation)
2. J. R.	2 years	2.53	(typhoid inoculation)
3. C. B.	6 months	2.57	(typhoid inoculation)
4. M. T.	15 months	2.60	(typhoid inoculation)
5. E. G.	6 months	2.65	(typhoid inoculation)
6. E. E.	16 months	2.98	
7. A. G.	9 months	2.93	
8. P. S.	4 months	2.98	
9. A. W.	15 months	3.00	
10. A. B.	2 years	3.05	
11. L. D.	4 months	3.05	
12. W. C.	14 months	3.09	
13. L. W.	4 months	3.06	
14. L. M.	2 years	3.14	
15. F. K.	6 months	3.15	
16. H. G.	2 years	3.27	
17. S. R.	14 months	3.51	
(b) Patients Who Showed Marked Improvement but Remained in the Hospital			
1. E. G.		2.52	(typhoid inoculation)
2. M. W.		2.75	(typhoid inoculation)
3. M. M.		2.91	
4. L. W.		2.95	
5. G. R.		2.97	
6. U. W.		3.08	
7. L. S.		3.08	
8. M. P.		3.10	
9. A. G.		3.15	
10. A. C.		3.17	

would hardly expect to find definite differences in the ratios along these lines. If the differences in the ratios are of any significance, their correlates must be looked for in some other aspects of the clinical picture and course. So far our study of the cases in which higher ratios appear as contrasted to those in which the ratios are normal have not yielded any definite facts. A few leads have been obtained, but they can be regarded only provisionally as useful suggestions and working hypotheses and not as definitely established facts. For instance, it seems noteworthy that we found a high percentage of normal ratios in patients whose condition has shown good remission without much appreciable defect. This is well illustrated by the list of cases diagnosed as schizophrenia; these patients were dismissed from the hospital when the condition was in good remission (table 2).

It can be seen from table 2 that of the twenty-seven cases in which good remissions or definite improvement occurred, only two showed distribution ratios above 3.2. Furthermore, in one of these, the figure can be regarded as borderline. In a good many of the cases that are somewhat puzzling (in that they show a perfectly typical schizophrenic reaction, generally of the acute catatonic type which pass on leaving the patient apparently at his previous level), the ratio tends to remain more within the normal limits.

At present we see no justification for making any more definite statements as to the value of the distribution ratio within the schizophrenic group. We have not been able to corroborate Walter's [5] statement that practically all cases in which the ratio was below 2.8 were either cyclothymic in type or old chronic cases of schizophrenia. If anything, the cases that in our investigations have shown a ratio below

TABLE 3.—*Distribution Ratio in Cases from the Literature Reported by von Rohden*

Author	Number of Cases	Distribution Ratio in Percentage		
		Low	Normal	High
Stoerring	65	3	19	78
Von Rohden	216	4	23	73
Kral	50	12	20	68
Buechler	62	21	19	60
Hauptmann	100	14	32	54
Kant-Mann	16	12	38	50
Jacobi-Kolle	25	4	48	48

2.8 have presented the picture which can be best described under White's [6] type of "decompensating schizophrenics." Whether or not the lack of resistance of the barrier may be associated with a lack of general resistance and the occurrence of a decompensating type of schizophrenia, remains to be discussed.

Very definite statements as to the value of the distribution ratio determination, in schizophrenias in particular, as well as in the different mental diseases in general, are furthermore premature, as there is still a variation among the figures reported by different observers. This is especially well seen from a review of the literature by von Rohden.[4]

In all cases reported in table 3 the ratios from 2.9 to 3.3 were taken as normal. In some cases it has been suggested even that from 2.9 to 3.5 should be taken as the normal limits. This, in our opinion, is unjustified in that the patients who were considered as normal by these authors were usually persons showing some kind of mental deviation. We have had only a limited experience with normal persons, but all

5. Walter, F. K.: Die Blut-Liquorschranke, Leipzig, G. Thieme, 1929.

6. White, W. A.: The Social Significance of Mental Disease, Arch. Neurol. & Psychiat. **22**:873 (Nov.) 1929.

of our cases fell very near the 3 line. In our previous communication, we stated our reasons for using from 2.8 to 3.2 as arbitrary limits of the normal. Within the hospital population, these limits can be taken as representative of a group of patients that remain between the two extremes. The advisability of taking these figures as an arbitrary middle is particularly well shown by the value of such a procedure in differential diagnosis. This is illustrated by table 4.

Table 4 needs no interpretation. We might add that the diagnoses, both the original as well as the final, were made independently of the distribution ratio determinations and the criteria utilized for diagnosis were the clinical course and final development of the disease process. Here too, of course, it is well to remember that an increased ratio is indicative, but not always pathognomonic, of schizophrenia, that it may

TABLE 4.—*Differential Diagnostic Value of the Determination of Distribution Ratio*

Name	Ratio	Original Diagnosis	Final Diagnosis
C. C.	395	Manic-depressive (manic)	Schizophrenia (catatonic)
G. W.	358	Manic-depressive (depressed)	Schizophrenia (catatonic)
A. V. S.	358	Manic-depressive (manic)	Schizophrenia (paranoid)
M. E.	354	Manic-depressive (depressed)	Schizophrenia (catatonic)
B. B.	336	Manic-depressive (depressed)	Schizophrenia (catatonic)
N. C.	331	Manic-depressive (manic)	Schizophrenia (catatonic)
H. M.	382	Undiagnosed psychosis	Schizophrenia (paranoid)
A. K.	330	Undiagnosed psychosis	Schizophrenia (catatonic)
A. C.	330	Undiagnosed psychosis	Schizophrenia (catatonic)
J. McC.	328	Undiagnosed psychosis	Schizophrenia (paranoid)
H. C.	364	Presenile psychosis	Schizophrenia (paranoid)
A. B.	305	Schizophrenia	Manic-depressive (depressed)
E. M.	275	Schizophrenia	Psychoneurosis
D. L.	236	Schizophrenia	Psychosis with encephalitis
S. F.	246	Schizophrenia	Toxic psychosis

occur in other conditions such as postencephalitic cases and in an occasional manic-depressive patient, and what is more important a large group of cases of schizophrenia show normal ratios. Just how large this group is and in what way it is related to those cases of schizophrenia that show a decreased passage for the bromides is a problem which will require further investigation.

The observations so far would seem to corroborate views that have been expressed by some authors on the heterogeneity of the schizophrenias. Such views, which hitherto have been based mainly on clinical and etiologic considerations, would seem to receive further support from the results reported here. We agree with Kafka [7] in his statement that as long as one deals with bromides only, one cannot speak of a generally lowered or increased resistance of the barrier between the blood and the cerebrospinal fluid. It is conceivable that

7. Kafka, V.: Das Problem der Function der Blut-Liquorschranke, Deutsche Ztschr. f. Nervenh. **105**:50, 1928.

in cases in which the bromide distribution is disturbed there may be no change in the ratio for other substances. There is, however, already some evidence in favor of the assumption that the bromides do not stand isolated in this respect. Guttmann,[8] for instance, has shown that in some cases of schizophrenia there is also a decreased rate of resorption of substances injected into the cerebrospinal fluid. This would point to a tightening of the barrier in both directions. The fact that in such cases the albumin of the cerebrospinal fluid may be increased, too, would not necessarily speak for a reduction of the resistance. As Kafka himself has brought out, these albumins may be produced within the cerebrospinal system and the increase may have to be explained on the basis of lessened resorption rather than an increased passage of substances. Furthermore, one must consider the fact that apparently the colloids and crystalloids do not depend on the same disturbances of the barrier.

Further proof that the behavior of the bromides in this respect is related to that of other substances was brought out by investigations carried on by one of us in cases of dementia paralytica.[9] It was found that the amount of iron in the walls of the cerebral vessels as well as in the tissues was closely correlated with the bromide distribution ratio as determined before death.

It does not lie within the scope of the present communication to discuss the possible mechanisms underlying the distribution of substances between the blood and the cerebrospinal fluid, or the relationship between the fluctuations in the resistance of the barrier and possible organic changes in the central nervous system. It seems, however, justifiable to emphasize those points which would serve as hints for the direction of further study. In previous investigations,[10] it was found that in certain organic vascular lesions there was a definite correlation between the condition of the vascular network of the cortex and the increased passage of bromides into the cerebrospinal fluid. Here we find that in a large proportion of schizophrenias there is a decrease in the amount of bromide passing through the barrier. Regardless of speculations as to any etiologic or pathogenetic relationship between such fluctuations in the ratio and the occurrence of the complicated psychic changes in schizophrenia, the observations reported justify a search for a basis of these fluctuations in the condition of the cerebral vascular network.

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8. Guttmann, L.: Ueber Stoerungen der Liquor-Resorption, Arch. f. Psychiat. **88**:211, 1929.

9. Malamud, W., and Wilson, R.: General Paresis Treated with Malaria, Arch. Neurol. & Psychiat. **22**:1135 (Dec.) 1929.

10. Malamud, W., and Lowenberg, K.: The Rôle Played by the Cerebral Capillaries in Pathogenesis of General Paralysis, J. Nerv. & Ment. Dis. **69**:121, 1929.

Further determinations on a large scale accompanied by studies in the clinical and neuropathologic fields will determine the real value of this highly promising method of approach.

SUMMARY

The results of the determination of the bromide distribution ratio between the blood and cerebrospinal fluid in 210 patients with schizophrenia are reported.

In schizophrenia uncomplicated by somatic diseases, 60 per cent of the cases show ratios above 3.2 (up to 4.3); 38 per cent, ratios between 2.8 and 3.2; 2 per cent, ratios below 2.8. This is true also of schizophrenic patients with a positive Wassermann reaction of the blood but no signs of neurosyphilis.

Active tuberculosis, cerebral arteriosclerosis, acute infections and reactions to typhoid inoculations tend to increase the passage of bromides into the cerebrospinal fluid (i. e., decrease the ratio).

No definite relationship was found between the distribution ratio and type of schizophrenia as usually classified.

A large proportion of cases of schizophrenia with ratios between 2.8 and 3.2 ran acute courses with good remissions.

The few cases (2 per cent) with a ratio below 2.8 showed passive decompensating types of schizophrenic processes.

A CROSSED FLEXION REFLEX OF THE UPPER EXTREMITY

SO-CALLED ABNORMAL ABDOMINAL REFLEXES *

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During the course of recovery from a partial Brown-Séquard paralysis, probably due to a localized meningomyelitis, an unusual crossed flexion reflex of the upper extremity was elicited by stimulation of the skin over the abdominal wall. The receptive field of this reflex extended from the sixth to the twelfth dorsal segment of the side opposite the lesion, and was included within the area in which, at the beginning, pain and temperature senses were completely lost between the second and twelfth dorsal segments.

The reflex could be elicited by firm scratching, pricking or the application of very hot or very cold stimuli. It was not elicited by tactile or other stimuli employed in testing so-called epicritic sensibilities.

The reflex consisted of a flexion of the wrist, semipronation of the forearm, flexion of the fingers and adduction and flexion of the thumb. The reaction time was short and the response prompt.

REPORT OF CASE

On May 6, 1924, a woman, aged 49, presented herself for examination. She gave a history of awakening one morning in January, 1924, with lessened strength in the left hand and pain in the shoulder and upper part of the left arm. She noted that attempts to bend the head forward were accompanied by twinges of pain in the shoulder and arm. The fingers of the left hand became numb. The pain subsided in two weeks, but the weakness in the fingers and wrist slowly increased so that at one time the hand was almost completely paralyzed for flexion. Wasting of the muscles of the hand and a peculiar feeling in the right abdominal wall were noted. No weakness was apparent in the left leg, and no bladder or rectal disturbances had been observed.

Examination.—The left hand presented the appearance of a claw hand, with the thumb in the plane of the palm. The hand was flexed at the wrist, the proximal phalanges were extended, and the distal phalanges were flexed. There was slight weakness of the flexors of the wrist and even less of the extensors; the pronators were slightly weak, and there was very little weakness in the extensors of the fingers. Moderate weakness was found in the extensor of the thumb; the index finger could be abducted slightly but not adducted. Very slight

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* From the Department of Nervous and Mental Diseases, Northwestern University Medical School.

abduction was present in the little finger; otherwise, no lateral movements were possible in the fingers. The adduction of the thumb was weak; the short abductor of the thumb and of the opponens were paralyzed. The distal phalanges could not be extended. There was an atrophy of the interossei and of the thenar and hypothenar eminences. All the muscles, with the exception of the opponens pollicis and the third and fourth interossei, responded to faradic stimulation if a very strong current was used. The muscles of the hypothenar eminence responded very slightly. To the galvanic current the contractions were definitely slower than normal. There was a spasticity in the flexors of the wrist, and very slight shortening had occurred in the muscles. There was very slight impairment of strength in the left lower extremity. The left pupil was smaller than the right, both reacting normally to light and in accommodation, and the palpebral fissure was smaller. The left biceps reflex was greater than the right; the left triceps was greater than the right. (One month later it was observed by another neurologist that the left triceps could not be obtained.) The ulnar jerks were equally brisk. The wrist jerk on the left was greater than that on the right. The knee reflexes were brisk, the left greater than the right, and the same was true of the achilles jerks. No pathologic reflexes were noted at this examination. The left lower abdominal reflex was absent, the right normal; the left upper was absent and the right upper was diminished. There was slight hypesthesia to touch, pain and temperature over the left little finger. From the second to the tenth dorsal segments of the right side there was a diminution of pain, heat and cold sensations. There was little difference in sensation in the lower extremities. The only area in which vibration sense was diminished was over the anterior superior spine. Roentgenograms of the cervical spine revealed only evidence of a slight arthritis.

Serologic examination of the blood and spinal fluid gave negative results, and a manometric estimation of the spinal fluid pressure showed a normal status. The cell count was normal, and no increase of protein was found. The Lange colloidal gold test was negative.

Course.—For a period of about four months the condition remained stationary, with the exception of increase of the area of diminished sensibility to pain and temperature to include the eleventh and twelfth dorsal segments. The condition then began to improve.

Crossed Flexion Reflex.—About September, 1925, when motor power had improved in all the muscles except the opponens pollicis and the lumbricales, and sensory loss to pain and temperature sense over the right second to tenth dorsal segments was far less than before, a peculiar reflex was observed. When the skin over the right second to tenth dorsal segments was stimulated by scratching, pricking, the faradic current or the application of very hot or cold tubes, the left forearm would pronate, the wrist, fingers and thumb flex and the thumb adduct. At times, stimulation as far as the first lumbar segment produced the reflex. Since that time the reflex has gradually diminished in force and at times is more easily elicited by the application of intense cold than pain.

For the most part the reflex movement occurred in the muscles which exhibited a spastic paresis and in which subsequent slight contracture developed. None of the ordinary abnormal ipsolateral cutaneous reflexes could be evoked in the affected upper extremity, and nociceptive stimuli applied to any part of this extremity failed to produce any reflex movement.

It is obvious that one is not dealing with an abdominal reflex, since the maximum motor response does not correspond to the level of area

stimulated, a characteristic feature of abdominal reflexes, as pointed out by Monrad-Krohn.[1] This is only an illustration of what Sherrington has called a "type reflex." In addition to this, a normal abdominal reflex was always elicited coincidentally with the abnormal crossed reflex of the upper extremity.

Monrad-Krohn [2] termed the reflexes obtained from stimulation of the abdominal wall, which are not true abdominal reflexes, "reflexes of different order." He described the reflex as occurring in three cases:

(1) A case of multiple sclerosis, in which the response was characterized by bilateral contraction of the abdominal wall, irrespective of the side stimulated, accompanied by an extension reflex of the lower extremities, more pronounced on the side stimulated. (2) A case of cerebrospinal syphilis, with pronounced weakness of both lower and the left upper extremities. In this case the abdominal reflex obtained from the left side was constantly accompanied by an extension reflex of the homolateral lower extremity and was bilateral. (3) This case, which he had reported before,[3] was one in which a tumor of the left centrum ovale produced a right hemiplegia. The contraction of the abdominal muscles was bilateral and at times was accompanied by slight flexion at the right hip and knee joint and at times at the right elbow.

That the abdominal wall may be included within the receptive field producing reflexes in the lower extremities has been known for a long time. Babinski, Jarkowski and Jumenti [4] described a case of Brown-Séquard paralysis in which stimulation of the abdominal wall produced defense reflexes in the homolateral lower extremity. Guillain [5] described a case of Brown-Séquard paralysis in which stimulation of the abdominal wall on the side of the lesion produced flexion of the great toe, and stimulation of the sole, extension.

Head and Riddoch [6] stated that in gross injuries of the spinal cord the abdominal reflex undergoes change. At first it may be possible to produce only a local segmental reflex. This gradually gives place to a vigorous general contraction of one half of the abdomen, and to this may

1. Monrad-Krohn, G. H.: Om obdominal reflexerne, Christiana, Steenski Bogtrykkeri, 1918.

2. Monrad-Krohn, G. H.: Reflexes of Different Order Elicitable from the Abdominal Region, Arch. Neurol. & Psychiat. **13**:750 (June) 1925.

3. Monrad-Krohn, G. H.: Contribution to the Question of a Possible Inversion of the Abdominal Reflex, Acta med. Scandinav. **54**:603, 1921.

4. Babinski, J.; Jarkowski, J., and Jumenti, J.: Syndrome de Brown-Séquard par coup de couteau, Rev. neurol. **22**:309, 1911.

5. Guillain, Georges: Syndrome de Brown-Séquard, Rev. neurol. **24**:625, 1912.

6. Head, Henry, and Riddoch, George: Studies in Neurology, London, Oxford Medical Publications, 1920, vol. 2, p. 467.

be added all of those phenomena in the lower extremity which otherwise follow scratching of the sole. Walshe,[7] in discussing the "flexion reflex of the lower limb," stated that when the reflex is well developed cutaneous stimuli applied to any part of the limb surface, and even to the lower part of the abdominal wall, will elicit a reflex complete in form.

The abdominal wall is included within the receptive area of the scratch reflex in spinal animals, as was shown by Sherrington.[8] In the normal guinea-pig, Graham Brown[9] pointed out that stroking of the lower part of the abdominal wall produced flexion in the lower extremities.

Irradiation of reflexes spreads more easily down than up the spinal cord, as was pointed out by Sherrington.[10] It is easier to obtain reflex movements of the limbs and tail by excitation of the skin of the pinna than the reverse. It is easier to elicit a movement of the hind leg by excitation of the fore leg than the reverse. It is not strange, therefore, that the most common irradiation from the receptive area of the abdominal wall is downward into the lower extremities. In contrast to many such observations, reflexes in the upper extremity have rarely been observed from stimulation of the abdominal wall.

Buzzard[11] reported a case of quadriplegia following injury of the spinal cord in the upper cervical region in which, after only a moderate paresis remained in the lower extremities and some recovery of sensation had taken place, scratching the skin between the second and sixth dorsal segments and over the inner aspect of the arm produced a sudden and vigorous thrust backward of the homolateral upper extremity which became extended, adducted, rotated inwardly, pronated and flexed at the wrist, and the fingers extended and adducted to make a cone.

In all of the reported cases the reflex in the upper extremity occurred on the homolateral side. In the case here reported the reflex was contralateral.

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7. Walshe, F. M. R.: The Physiological Significance of the Reflex Phenomena in Spastic Paralysis of the Lower Limbs, Brain **37**:269, 1914-1915.

8. Sherrington, C. S.: Observations on the Scratch Reflex in the Spinal Dog, J. Physiol. **34**:1, 1906.

9. Brown, T. Graham: Studies in the Physiology of the Nervous System: VIII. Neural Balance and Reflex Reversal with a Note on Progression in the Decerebrate Guinea Pig, Quart. J. Exper. Physiol. **4**:273, 1911.

10. Sherrington, C. S.: The Integrative Action of the Nervous System, New Haven, Conn., Yale University Press, 1923.

11. Buzzard, E. Farquhar: Case of Spastic Paraplegia Following Injury of the Spinal Cord in the Upper Cervical Region, Showing Certain Unusual Reflex Phenomena, Brain **42**:364, 1919.

Contralateral reflexes in the lower extremities are well known. The reflex commonly is in the form of contralateral extension, and the crossed flexion response has been shown by Walshe [7] to be a part of a crossed extension reflex. Actual crossed flexor responses in man are found, however, as shown by McNamara and Gunson,[12] in the crossed flexor response to grasping the thigh in certain, chiefly cerebral, lesions.

In gross injuries of the spinal cord with mass reflexes, there is an exception to the general rule laid down by Sherrington, that in the hind limbs of the spinal animal simultaneous reflex movements are opposite in phase in the two limbs. The same is true in paraplegia in flexion and in conditions transitional between this and the extensor forms of spastic paralysis in which, as pointed out by Walshe, "We do see a crossed flexion reflex with its integral extensor response."

Graham Brown [9] has shown that the reaction of a limb to a reflex is dependent, among other things, on the neural balance that is produced by the general play of center on center. The receptive field, the character of the stimuli, the passively assumed position of the extremities and particularly the actively assumed position of the extremities, the play of labyrinthine and neck tonic reflexes, all contribute in determining whether a spinal reflex will be all flexor, all extensor or combined.

Béritoff [13] has shown that, when in the ipsolateral flexor effect of the decerebrate preparation it often occurs that contraction appears in the extensors as well, it is due to augmentation of tone by labyrinthine tonic reflexes.

Monrad-Krohn considered the "reflexes of a different order" as "reflexes of spinal (mesencephalic) automatism."

Marie and Foix [14] regarded all the reflexes of the spastic lower limbs as evidence of spinal function liberated from cerebral control and regarded them as analogous to movements representing the mechanism of locomotion. Babinski, however, regarded them as defensive, with which view Walshe is in accord.

As Head pointed out, Marie and Foix were dealing with a different group of cases from those on which he had based his own argument on the "mass reflex." He expressed the belief that as long as local reflex signature is not destroyed and as long as primary postural reflexes can be obtained, the lower end of the spinal cord has not been liberated from the control of the parts above the lesion.

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12. McNamara, E. D., and Gunson, E. B.: Some Cases of a Crossed Reflex Associated with Pain: The Bearing of the Crossed Reflex upon the Theory of the Existence of Automatic Spinal Centers, Brain **37**:409, 1914-1915.

13. Béritoff, J. S.: On the Reciprocal Innervation in Tonic Reflexes from the Labyrinth and the Neck, J. Physiol. **49**:147, 1924.

14. Marie, P., and Foix, C.: Les réflexes d'automatisme médullaire, Rev. neurol. **23**:657, 1912.

In the work on decerebrate rigidity done with Loyal Davis,[15] it appeared to me that the pattern of a reflex is dependent on the interplay of all other neural activities. When tone is heightened in a certain group of muscles, certain patterns appear as extension. When this tone is destroyed, as in a labyrinthless animal, other patterns appear. This corresponds closely to Graham Brown's conception of neural balance. In the case here reported, it is difficult to ascribe a protective mechanism to the particular pattern of the crossed reflex. It is equally difficult to classify the movement as one of spinal automatism, particularly as voluntary movement was possible in the muscles participating in the reflex.

Two observations seem pertinent: 1. The reflex occurred in the muscles in which heightened tone could be demonstrated. 2. The reflex occurred as the result of stimulation of a zone possessing abnormal sensibility.

Nocuous impulses are carried by the fibers conveying so-called protopathic sensibility. It is well known that overresponse to sensory stimuli is common in cases in which the area stimulated is imperfectly supplied with sensation. Such cases may be found in thalamic lesions, as pointed out by Holmes and Head,[16] who attributed the overreaction to a loss of cortical control to the thalamus. Spiller[17] found similar reactions to peripheral stimuli in cases of disease below the optic thalamus, one a lesion of the medulla producing analgesia in the fifth nerve, another a lesion in the right side of the pons or medulla in which disturbed objective sensation in the right fifth nerve was present, with hypesthesia to pain and temperature throughout the entire left half of the body, and on this side a marked overreaction to sensory stimuli was observed.

Weisenburg and Stack,[18] in a patient who at necropsy was found to be suffering from a tuberculoma of the right side of the tegmentum of the pons, and who prior to death had impaired sense of position and diminished heat, cold and tactile sensibility as well as pain, observed that he experienced discomfort from such stimuli, and when pricked by a pin, though pain sense was diminished, had marked paresthesia. Similar overreaction occurs from stimulation of the area of overlap in peripheral nerve lesions in which the only sensations felt are those produced by so-called protopathic sensibility.

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15. Pollock, Lewis J., and Davis, Loyal: Studies in Decerebration: V. The Influence of the Cerebellum upon Reflex Activities, Baltimore, Williams & Wilkins Company, 1929.

16. Holmes, Gordon, and Head, Henry: Studies in Neurology, New York, Oxford University Press, vol. 2.

17. Spiller, William G.: Central Pain in Syringomyelia and Dysesthesia and Over-Reaction to Sensory Stimuli in Lesions Below the Optic Thalamus, Arch. Neurol. & Psychiat. **10**:491 (Nov.) 1923.

18. Weisenburg, T. H., and Stack, S. S.: Central Pain from Lesions of the Pons, Arch. Neurol. & Psychiat. **10**:500 (Nov.) 1923.

It appears clear that this overresponse is due not alone to the removal of cortical influence on the thalamus, but to a disturbance of neural balance in relation to sensation, just as has been shown to be the case in relation to motion. Common to all of these examples of overreaction is the imperfect sensibility of the cutaneous area, especially as concerns pain sense. Touch may be entirely lost or almost perfectly conserved, but epicritic painful sensibility is always rather profoundly disturbed.

It is evident that the disturbance of neural balance in the motor field expressed by the hypertonicity of the muscles participating in the reflex was not alone responsible for the reflex, else it would have been elicited by stimulation of the homolateral upper extremity. An additional peculiar stimulus was necessary, and this was supplied by the stimulation of the opposite abdominal wall, from which fibers carrying so-called protopathic sensibility crossed in an ascending manner to activate the motor cells of the cervical segments.

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DISCUSSION

DR. S. W. RANSON: The usual rule for reflexes in the decerebrate animal is that stimulation of one limb causes that leg to flex and the opposite one to extend. But as Graham Brown and Sherrington showed, in 1912, this rule is subject to exceptions. In some work that Dr. Hinsey and I have been doing on decerebrated cats we have found, in agreement with Graham Brown, that for the crossed response there is a dilemma of reaction, and the stimulation may cause either flexion or extension of the opposite leg. The crossed reflex is variable. It may be a pure extension, but more often involves some contraction of the flexor muscles. It may be pure flexion or the flexion may be followed by an extensor rebound. Weak stimulation will often produce crossed extension when strong stimulation will cause crossed flexion. We have, in these animals, something that is at least akin to the crossed flexion reflex that Dr. Pollock has found in the human forearm.

PRODUCTION OF SLEEP AND REST IN PSYCHOTIC CASES

A PRELIMINARY REPORT *

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This preliminary report deals with the intravenous use of sodium isoamylethylbarbiturate in the production of sleep and physical rest in psychotic patients. Since the days of Weir Mitchell, investigators have continued to search for ways to promote these essential measures in the treatment of the psychoses. For the past ten years, at the Wisconsin Psychiatric Institute, many drugs have been studied under the direction of Dr. W. F. Lorenz, especially those that might be effective in acute mental excitements and agitated depressions.

The derivatives of barbituric acid have been known to possess anesthetic and analgesic properties, when administered orally and intraperitoneally (Page,[1] Tatum and Parsons [2]), with little effect on blood pressure and no influence on the concentration of blood sugar. Page and Coryllos [3] prepared the sodium salt of isoamylethylbarbituric acid and used it intravenously in dogs. They found that a dose of from 40 to 50 mg. per kilogram of body weight was effective for general anesthesia. This was associated with a slight temporary fall in blood pressure. Gruber and Roberts [4] showed that the derivatives of barbituric acid caused an increased coronary flow and a fall of blood pressure of more than 40 mm. in dogs, and he believed that this was due to vasodilatation. They also found a definite dilatation of the

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1. Page, I. H.: Iso-Amyl-Ethyl Barbituric Acid, an Anesthetic without Influence on Blood Sugar Regulation, J. Lab. & Clin. Med. **9**:194, 1923.

2. Tatum, A., and Parsons: Barbital as an Anesthetic in Dogs, J. Lab. & Clin. Med. **8**:64, 1923.

3. Page, I. H., and Coryllos, A.: Iso-Amyl-Ethyl Barbituric Acid (Amytal), Its Use as an Intravenous Anesthetic, J. Pharmacol. & Exper. Therap. **27**:189, 1926.

4. Gruber, C. M., and Roberts, S. J.: Effect of Sodium Phenobarbital and Some Other Barbituric Acid Derivatives upon the Coronary Circulation, J. Pharmacol. & Exper. Therap. **27**:319, 1926; Effect of Phenobarbital and Some Other Barbituric Acid Derivatives upon the Cerebral Circulation, ibid. **27**:349, 1926.

cerebral vessels, which they attributed to the direct effect of the drug on the walls of the blood vessels.

Loevenhart and his associates [5] showed that sodium isoamylethylbarbiturate was most effective in preventing a fatal outcome in acute intoxications with cocaine and its derivatives.

Following the recent work and excellent results obtained in the field of surgical anesthesia in man by Zerfas, McCallum and their coworkers,[6] I undertook the study of sodium isoamylethylbarbiturate in the treatment of patients with psychoses. All types of mental excitement and depression were included in this study. Over fifty cases were studied, and more than 150 injections were administered.

METHOD

The method advocated by Zerfas and his associates [6] was carefully followed. The calculated dose for the body weight was dissolved in triple distilled water, immediately before administration, to make a solution of 5 per cent strength. It was gently agitated until all crystals had dissolved and it was water clear; an opalescent solution was discarded. The prescribed dose was then injected intravenously very slowly, so as not to exceed 1 cc. per minute. This procedure was carried out with the stomach empty, as patients occasionally become nauseated; I know of two cases of drowning from the aspiration of vomitus. In this study, the patient was never left alone until the initial narcosis had disappeared.

DOSAGE

The problem of dosage in the psychoses is different from that in surgical anesthesia. Shortly after starting this work, it was found that dosage is individual, and further, that in the exhaustive mental states a smaller dose is effective and less hazardous. About one-half the dose used in obtaining surgical anesthesia suffices for the most part in producing sleep in psychotic patients. For anesthesia, doses of from 15 to 25 grains (0.96 to 1.6 Gm.) have been used.[6] In most of the cases reported here, the patients responded to from 7 to 15 grains (0.45 to 0.96 Gm.). Another point of difference in producing sleep in a psychotic patient as compared with securing surgical anesthesia is the need for repeated doses. Repetition of the dose is necessary in order that the desired state of sleep and relaxation may be maintained over a longer period of time. In some of the cases reported the patients were

5. Knoefel; Herwick, and Loevenhart: Proceedings of American Society for Pharmacology and Experimental Therapeutics, J. Pharmacol. & Exper. Therap. **32**:265, 1928.

6. Zerfas, L. G.; McCallum, J. T.; Shonle, H. A.; Swanson, E. E.; Scott, J. P., and Clowes, G. H. A.: Induction of Anesthesia in Man by Intravenous Injection of Sodium Iso-Amyl-Ethyl Barbiturate, Proc. Soc. Exper. Biol. & Med. **26**:399, 1929; Zerfas, L. G., and McCallum, J. T.: J. Indiana M. A. **22**:47, 1929.

treated daily for from eight to ten days. For these patients, the second and subsequent doses were determined by the duration of the response to the initial dose and by whether or not the patients took sufficient nourishment and fluid during the period of the drug's effect. Some patients were permitted to rouse themselves to the former states of mental activity before the induction of sleep was again attempted.

Unfinished work, to be reported at a later date, is the application of intramuscular and oral therapy after the initial use of the intravenous injection. It is anticipated that these methods will permit the use of the drug for a longer time without necessitating the deep narcosis produced by the intravenous route.

A criterion has been established for the initial dose in all cases. This is based on the abolition of the corneal reflex. Three grains (0.19 Gm.) more are given than is necessary to produce corneal anesthesia; this has been found to be a safe initial dose.

CLINICAL OBSERVATIONS

Every patient in my series, regardless of the degree of excitement, became drowsy after 3 cc., or 4½ grains (0.28 Gm.), had been injected. He might yawn once or twice, or cough. After from 7½ to 10 grains (0.48 to 0.64 Gm.) had been administered, he usually was in profound sleep. The deep and superficial reflexes disappeared, the pupils dilated, and the corneal reflex was abolished.

At this time, the respiratory excursion became shallow, and the rate was slightly increased. This continued for about three or four minutes. There was no pallor, cyanosis or appearance of collapse. The pulse rate was accelerated by from 10 to 12 beats. There was a suggestion of vasodilatation in some cases. In these, the patient's color seemed better than before the injection was started.

The blood pressure changed from the time of administration. Contrary to all previous reports, possibly owing to the nature of the cases treated, although several normal persons were included, I found that the systolic pressure continued to fall for more than thirty minutes. In some cases, it fell for almost an hour. The systolic pressure dropped from 20 to 88 mm. The diastolic pressure fell, but to a much less degree, namely, from 2 to 30 mm. There was a tendency toward parallelism of the two pressures. In two cases, the pulse pressure fell below 20 mm. This will be commented on elsewhere. In every instance, the blood pressure returned toward normal after one hour, and usually reached normal before two hours had elapsed.

The corneal reflex usually reappeared after from twenty to forty minutes, and the deep reflexes followed. After about an hour, the patient responded to painful stimuli, but with a marked delay in the reaction time.

The profound sleep lasted for from two to eight hours and seemed in a measure to be determined by the type of case rather than by the size of the dose. This impression resulted from the similarity of the sleep curves obtained in those cases in which varying doses were given on consecutive days.

It was common, after two or three hours, to have the patient turn from one side to the other. Occasionally, the patient roused to take fluids and nourishment and then went back to sleep for several hours. Several patients were aroused deliberately; they took fluids and nourishment automatically; then arranged the pillows and covers and went back to sleep.

On the return to consciousness there was a prolonged period of physical relaxation and drowsiness. This again was variable and lasted from two to six hours, during which the patients took more nourishment. This period was usually followed by several hours of normal sleep without any more drug. This observation is the most important one made in the study. I believe that the normal sleep following the period of drowsiness is the most desirable effect obtained by means of this drug. I saw no evidence of an exaggerated excitement when the patient had recovered from the sleep, as has been seen in animals following anesthesia.

PSYCHIATRIC OBSERVATIONS

The most violently disturbed patient was precipitated into a profound sleep as readily as a normal person. In all my cases, the patient was asleep within five minutes of the time when administration of the drug was started. The patients with the more exhaustive types of disorder were asleep in from three to four minutes. In a few cases there was a lucid interval for one or two minutes just before the patient went to sleep. During this short interval, the patient was rational and had complete insight into his condition. This was true in case 3 of catatonic excitement.

Patients who were aroused spontaneously or deliberately during the initial sleep showed a typically alcoholic appearance—speech was stumbling, slow and thick; the eyelids drooped, and there was marked incoordination of physical movement.

As the initial sleep wore off, the patient appeared dazed; the eyes were half open and there was apparently little active cerebration. The patient responded to commands automatically and with a slow reaction time. It was during this stage that in several cases of catatonic dementia praecox the patients had striking periods of normal existence. In three of these, the lucid interval lasted for from two to fourteen hours. The patients asked questions and answered others; they discussed football scores, the duration of the illness, family and relatives,

and took nourishment. One of these patients had been fed by tube for two years (case 1); another for four months (case 2).

All patients, whether previously depressed or excited, as they came out of the initial period of sleep, seemed calm and collected; also they were emotionally stable. The thought content was apparently clear, and expressions were coherent and relevant.

A very desirable period of sleep followed this state of drowsiness. Since all administrations of the drug were made in the forenoon, it is thought that this second period of sleep resulted from the continued effect of the drug during the early part of the night when the noises and ordinary stimuli of the hospital were at a minimum.

In nearly all cases there was a gradual return toward the previous mental condition after from twelve to eighteen hours. In many cases, however, the patient never returned completely to the same degree of mental excitement; several patients recovered rapidly.

REPORT OF CASES

A few cases are incorporated to typify the reaction for certain groups of mental excitement.

CASE 1.—A. G., aged 35, weighing 66 pounds (29.9 Kg.), with catatonic dementia praecox, had been fed by tube for over two years. She had received at least ten anesthesias with carbon dioxide and oxygen (Lorenz and his associates[7]) about one year before coming to the hospital, after each of which she talked normally for from five to fifteen minutes and then sank back into catatonia.

She was given 7½ grains (0.48 Gm.) of sodium isoamylethylbarbiturate, and she slept for four hours. She answered questions for two hours; she told me that she had missed her own physician while she was in Europe for six months (a fact); she was perfectly oriented as to time, place and person; she recalled the anesthesia with carbon dioxide and oxygen a year previously; she had perfect memory and insight. She refused, however, to take food and was fed by tube. She slept all night. She awakened at 6 a. m. and said that she was going to die. She was fed by tube and showed a similar response on the next day. This patient was unable to relax completely because of muscular contractures.

CASE 2.—T. W., aged 33, had catatonic dementia praecox. The onset occurred with delusions and hallucinations one year before, following a pregnancy. She became disturbed and attempted to run away from home; later, she was stubborn and resistive and refused food. She lost weight from 130 to 80 pounds (59 to 36.3 Kg.) in six months. For four months, she had been in a cataleptic stupor and had been fed by tube.

Seven and one-half grains (0.48 Gm.) of sodium isoamylethylbarbiturate was administered intravenously. The patient slept for four hours, and was drowsy for three and one-half hours; then she asked for a glass of water and took a glass of milk. She asked the score of a football game that was being played on that afternoon; she asked also for her baby and wanted to talk to

7. Loevenhart, A. S.; Lorenz, W. F., and Waters, R.: Cerebral Stimulation, J. A. M. A. **92**:880 (March 16) 1929.

her husband. She continued to talk normally for almost an hour, then lay down fully relaxed and went to sleep for four hours. When awake, she was negativistic, but not cataleptic. She was given daily doses. She argued against venipuncture. She was fed by tube when asleep, but took considerable nourishment while awake. She said that the stomach tube burned her throat and upset her stomach.

Case 3.—J. L., aged 20, a university student, had catatonic excitement, which had had a sudden onset with confusion and mutism and refusal of food; after three weeks he went into a state of marked excitement with active hallucinations and bizarre gesticulations and grimaces. He set fire to his bed and yelled "fire."

He was given 10 grains of sodium isoamylethylbarbiturate. Just before he went to sleep he said that he realized he was having a terrible time and hoped to recover to enter school in February. When he came out of the sleep, he behaved in a normal way, and discussed current topics, his illness, school and his future plans. This lucid interval lasted for almost two hours. After a short sleep, he returned to an excited state. At the time of writing, he had made similar responses after further treatment and was less hyperactive.

Case 4.—C. B., aged 30, weighing 118 pounds (53.5 Kg.), was suffering from a manic-depressive psychosis—manic phase—that had lasted three months. She had had one previous similar attack. She was very talkative, sang and swore. Physically, she was active and pugnacious.

She received 7½ grains of sodium isoamylethylbarbiturate, and felt dizzy as she went to sleep. She slept for two hours and then awoke. She took nourishment, fussed with her hair and shook her head. She again slept two hours, and then took a pint of water, jumped on the bed, rolled over and slept for one hour. She then awoke and said that she felt fine and was going home. She quieted down and dozed from time to time until midnight (eight hours); then she was playful, uncovered other patients, and finally went to sleep again until morning. When she awoke, she was quiet. On the second day, she made a similar response to therapy, but without the frequent interruptive flights. This is believed to have been due to her removal from the dormitory where another excited manic patient was being given a course of sodium isoamylethylbarbiturate by mouth, whose outbursts had roused her on the first day.

Case 5.—S. K., aged 38, weighing 140 pounds (63.5 Kg.), had a manic-depressive psychosis—manic phase—that had lasted three weeks. A history of her past life and of two similar attacks was obtained only after the patient came out of the first day's sleep. She was noisy, required restraint, used vile language and spat at everybody. She slept for only one and one-half hours after being given 1 ounce (30 cc.) of paraldehyde. Ten days of hydrotherapy were without results.

She was given 10 grains (0.64 Gm.) of sodium isoamylethylbarbiturate. She slept two and one-half hours, relaxed for three hours, was normal for one and one-half hours and then gradually became restless, but merely sang, prayed and recited poetry. Restraint was unnecessary. She slept for seven hours without any drug. This patient received a daily dose for ten days; then her husband took her home, against advice, because he thought that she was well enough to take care of five children.

Case 6.—J. P., aged 28, weighing 150 pounds (68 Kg.), presented a manic-depressive psychosis—manic phase—three days after an appendectomy. He became violent and noisy, sang, screamed, swore, tore out electric light fixtures and bed linens and became unmanageable. This continued for one week in spite of

all sedatives and hypnotics. He was transferred to the neuropsychiatric service of the hospital.

He received 15 grains (0.96 Gm.) of sodium isoamylethylbarbiturate. He slept for eight hours, awakened and seemed confused and irrational, but quiet, for two hours; he then fell asleep for six hours and on waking was normal. He remained normal for ten days and was discharged. On recovery he said that he had had four or five previous manic episodes, of much longer duration, during a period of ten years.

CASE 7.—M. H., aged 52, weighing 85 pounds (38.6 Kg.), with an agitated depression of the involutional period, had been depressed for about six months, with crying, anxieties, self depreciation and delusions of infidelity; finally, three weeks before admission to the hospital, she became maniacal and required restraint. She was very loud, and showed a flight of ideas and marked suggestibility; she sang, was hoarse from screaming and was physically very active.

She received daily doses of 7½ grains (0.48 Gm.) of sodium isoamylethylbarbiturate. After the first twenty-four hours, restraint was unnecessary. She averaged about ten or twelve hours of sleep; eight hours of being normal or drowsy and relaxed, and from four to six hours of mild excitement. This gradually subsided, and after eight days she was perfectly normal.

CASE 8.—H. C., aged 50, weighing 190 pounds (86.2 Kg.), was brought in as an emergency case in a semidelirious condition from acute alcoholic psychosis. He was said to have taken a large amount of denatured alcohol. It was impossible to pass a stomach tube or to treat him because of his physical strength and violence.

He was given 10 grains (0.64 Gm.) of isoamylethylbarbiturate, after which no difficulty was encountered in washing out his stomach or in the use of other therapeutic measures. He was easily controlled during the entire period of his delirium.

CASE 9.—A. J., aged 14, weighing 110 pounds (49.9 Kg.), had status epilepticus from a tumor of the brain. Jacksonian convulsions of the left side of the face and arm developed, the twitching continuing for thirty minutes. This spread into a general grand mal convulsion, and successive convulsions occurred for four hours. In spite of morphine, ¼ grain (0.016 Gm.), sodium bromide, 40 grains (2.56 Gm.), and inhalations of ether and chloroform, the seizures persisted. The temperature rose to 104 F.; the pulse rate was 160; respirations were irregular. Artificial respiration had been instituted eight times in the previous hour. Pulmonary edema and cyanosis developed and the lad was becoming rapidly exhausted.

Atropine sulphate, 1/75 grain (0.8 mg.), was administered, and 10 grains (0.64 Gm.) of sodium isoamylethylbarbiturate. The patient immediately fell into a profound sleep. The twitching stopped after 5 grains (0.32 Gm.) had been injected. The breathing was shallow and stopped once, but responded to artificial respiration. The pulse and respiration became regular in thirty minutes. The patient slept for three and one-half hours, and after five and one-half hours similar jacksonian attacks developed. This continued for two hours. Ten grains (0.64 Gm.) of sodium isoamylethylbarbiturate was again administered, and the patient slept for another five and one-half hours; when he awoke he was normal with normal temperature, pulse and respiration. There is not the slightest doubt but that the drug was a life-saving measure in this case.

CASE 10.—J. F., a woman, aged 63, weighing 120 pounds (54.4 Kg.), with an arteriosclerotic psychosis, was one of two patients in whom certain physical phenomena occurred which are looked on as hazardous, and was the type of

patient who is considered a poor risk for this procedure. She was worried, and whined and cried continuously.

She received 7½ grains (0.48 Gm.) of the drug. The systolic blood pressure fell to 74 and the diastolic to 62 in forty minutes. In spite of a pulse pressure of only 12, there was no cyanosis or pallor; respirations, 22 per minute, were shallow, but regular. The patient was treated for shock and given epinephrine hydrochloride and caffeine; in twenty minutes the systolic pressure was 92; the diastolic, 60. The mental picture following recovery was identical with the original picture.

Comment.—It is believed positively that generalized arteriosclerosis with suspected myocarditis is a poor risk for this procedure and should be considered as a contraindication to its use.

SUMMARY

1. Sodium isoamylethylbarbiturate was used intravenously in over fifty cases of all types of psychosis. Patients with all types of mental excitement and agitation fell into profound sleep from its use. Sleep and physical and mental relaxation lasted from twelve to eighteen hours following one injection. The normal sleep following the period of relaxation was the most desirable result obtained in the treatment of acute manias with sodium isoamylethylbarbiturate.

2. The dose varied in individual cases; it averaged from 7 to 15 grains. Repeated daily doses were effective in several cases.

3. Blood pressure continued to fall in the first hour following injection and the fall was greater than has been previously reported. As a routine, blood pressure was taken every fifteen minutes until it returned to normal.

4. Feeding by tube and the handling of patients with acute delirium were made easy by this method.

5. Narcosis had to be induced on an empty stomach, and the patient had to be watched until the initial narcosis disappeared.

CONCLUSIONS

1. Sodium isoamylethylbarbiturate is extremely valuable in controlling sleep associated with the excited mental states.

2. With its use, more rapid early recoveries can be anticipated in the acute manias.

3. Normal lucid intervals with spontaneous speech and the taking of nourishment are seen in protracted cases of catatonic dementia praecox.

4. Status epilepticus and acute deliriums can be controlled by the intravenous injection of sodium isoamylethylbarbiturate.

5. Sodium isoamylethylbarbiturate intravenously injected causes a pronounced reduction of blood pressure in mental cases.

6. The intravenous injection of sodium isoamylethylbarbiturate is contraindicated in advanced myocarditis or generalized arteriosclerosis.

JUSTIFICATIONS FOR AND RESULTS OF EXPLORATORY LAMINECTOMY *

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An exploratory operation is a confession, if not of ignorance, at least of incomplete knowledge. Strictly speaking, almost every operation is an exploration, and even when one is most certain of the underlying condition, surprises may be encountered. But as commonly used, the term "exploration" implies uncertainty. The uncertainty may apply to the actual presence of a lesion or only to the nature or extent of the lesion. In the latter sense, the exploration is performed to determine whether or not the disease is remediable by surgery.

In the development of any branch of surgery, progress reduces the number of exploratory operations. Analysis of the history of the patient correlated with the physical signs plus the aid from various laboratory studies increases the probability of a correct diagnosis. But in the early stages, no little help is contributed by the surgeon through exploratory operations.

Through improved methods of investigation, such as manometric determination of a block or partial block of the cerebrospinal fluid, the use of iodized poppy seed oil 40 per cent for contrast roentgenography and the estimation of the protein content of the cerebrospinal fluid, the qualification of laminectomy by the term "exploratory" is becoming less frequent. There are, however, instances in which in spite of all investigations one is not able to state that the patient is not suffering from a lesion remediable by surgical measures. In a series of 140 laminectomies reported by Sachs and Glaser,[1] there were 33 in which no tumor was found. These included five cases in which the cord and meninges appeared normal, nine cases in which the cord was normal and the meninges pathologic, seven cases in which the cord appeared pathologic and the meninges normal, and twelve in which both cord and meninges seemed diseased. Schönbauer,[2] in an analysis of ninety laminectomies done in the course of twenty-five years, stated that in twenty-four cases no tumor was found.

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* From the Neuro-Surgical and Neurological Services of the Mount Sinai Hospital.

1. Sachs, E., and Glaser, M. A.: Definite Level Symptoms Suggesting Spinal Tumor, J. A. M. A. **88**:308 (Jan. 29) 1927.

2. Schönbauer, L.: Die Ergebnisse der operativen Behandlung der Rückenmarkstumoren, Arch. f. klin. Chir. **154**:645, 1929.

During the past four years, twelve patients were subjected to exploratory laminectomy without disclosing a remediable lesion. In one case, the preoperative diagnosis was epidural abscess; in eleven, the exploration was done for a suspected tumor. I have not included in this group any case of well marked arachnoiditis, although there were several instances of this condition in the period covered. With the exception of the cord in case 2, which presented a nevus, the diagnosis of which was suggested preoperatively because of multiple nevi of the body, no cord showed grossly any lesion to explain the level localization. When the exploration was extended upward or downward, the appearance of the cord was uniform. There was always a free flow of cerebrospinal fluid. There were at times a few filmy subarachnoid strands in the operative field. These of themselves did not seem sufficient to explain the signs or symptoms. They were not of sufficient density to fix the cord as suggested by Stookey [3] in his paper on arachnoiditis. Whether they were external evidence of an intramedullary inflammatory process I am not prepared to state.

The first of the instances to be described was undoubtedly one of an inflammatory process. The preoperative diagnosis was epidural abscess.

REPORT OF CASES

CASE 1.—*A woman with quadriplegia after incision and drainage of a cervical abscess. Negative cervical laminectomy six weeks after the onset. Recovery.*

History.—M. S., aged 30, was admitted on Aug. 6, and discharged on Nov. 24, 1928. Five weeks prior to admission, she had had an incision and drainage of an abscess of the postcervical region. A week later, she first experienced difficulty in walking because of weakness of both legs. At this time she also noted that there was some weakness of the right arm, in which she suffered burning pain.

Examination.—The patient showed a discharging sinus on the right side of the neck posteriorly, which did not extend to bone. The neck was held rigidly. There was weakness of the right upper extremity, and the grip of the left hand was weak. The thenar eminences of both sides were atrophied. Both lower extremities were weak, the right more than the left. All deep reflexes were exaggerated, more on the right side. The left lower abdominal reflex only was elicited. There was a bilateral Babinski response. Sensory changes were present, but no definite level could be established; it seemed to be between the seventh cervical and the second thoracic segments. There was no block on manometric determination. The spinal fluid contained 3 cells. The Wassermann reaction of both blood and spinal fluid was negative. During a three day observation, the temperature fluctuated between 100 and 101 F.

Course and Operation.—A provisional diagnosis of epidural abscess was made, and on August 9, a laminectomy of cervical vertebrae 4, 5, 6 and 7 was performed. A slight thickening of the dura opposite cervical vertebra 7 was the only patho-

3. Stookey, B.: Adhesive Spinal Arachnoiditis Simulating Spinal Cord Tumor, Arch. Neurol. & Psychiat. **17**:151 (Feb.) 1927.

logic observation. The postoperative course was one of continued improvement, beginning about a week after the operation. A month following the operation, an unexplained low grade papilledema appeared, but soon receded. One year after the operation, there was a suggestion of weakness of the right upper and lower extremities and no other neurologic signs.

Although in case 2 the suggested preoperative diagnosis was substantiated, the condition was one in which radical surgery would probably have done harm.

CASE 2.—*A woman with progressive weakness of the legs and paresthesias showed two ill defined sensory levels, and multiple telangiectases scattered over the body. A laminectomy disclosed a nevus. Subjective postoperative improvement.*

History.—K. G., a woman, aged 51, complained of paresthesias in both legs associated with progressive weakness of seven months' duration. The trouble began as a gnawing pain in the left foot; soon it involved the right foot and spread up the legs. Weakness of the legs appeared and progressed to the point where the patient walked without lifting either foot from the ground. There was some difficulty in initiating urination.

Examination.—Atrophy of the musculature of the left thigh and leg was noted. There was bilateral weakness of the lower extremities, more marked on the left side. The deep reflexes in the left lower extremity were exaggerated, as was the right ankle jerk. The abdominal reflexes were all absent; there was no Babinski response. A sensory examination showed patchy areas of anesthesia, more extensive on the right, with ill-defined sensory levels at the sixth thoracic and the fourth cervical segments. Vibratory sense was lost on the left. Manometric determination showed no block. A few drops of iodized oil were arrested at the tenth thoracic vertebra. Telangiectases were scattered over the trunk. These, in combination with the several levels, suggested similar multiple lesions of the cord.

Operation and Course.—A laminectomy, on March 8, 1929, of the tenth, eleventh and twelfth thoracic vertebrae showed a nevus on the dorsal and left lateral aspect of the cord. It extended over one and a half cord segments, many of the vascular loops waving freely in the subarachnoid space. The patient received postoperative radiotherapy. Four months after the operation, the patient showed marked subjective improvement and walked better, but examination showed practically no change in the physical signs.

A summary of the twelve cases will be found in the accompanying table. Analysis of these cases shows that sufficient evidence was found to classify eleven of them as possible cases of tumor. From the standpoint of the history, the shortest time from onset to entrance into the hospital was nine weeks. This was in the case of a patient who suffered from a lesion of the cauda equina. The time is rather brief, especially for a tumor in this location, but tumors of the cauda equina with two months' history have been reported. The longest time from onset to hospitalization was seven years, which is well within any outside limits for a history of tumor. The time element in the other cases closely approximates the usual time element in the history of patients with

Clinical Summary of Cases

	Hospital Number	Age and Sex	Onset	Prior to Operation	Course	Chief Complaints	Main Signs	Queckenstedt	Iodized Oil and X-Rays	Operator, Site of Laminectomy and Observations	Results and Follow-Up	Remarks
1	223468	30 F	Sudden	5 weeks	Progressive	Weakness of both legs and right arm one week after drainage of cervical abscess	Paresis of both legs and right arm; increased deep reflexes; sensation diminished below C 7; sinus in neck; fever 101 F.	Negative	.....	Cohen (8/8/28) C 4, 5, 6, 7; some thickening of dura at C 7	Postoperative improvement; 12 mo. later slight residual weakness of right side	Possibly infectious myelitis
2	236148	51 F	Gradual	7 months	Progressive	Formication; pain in and weakness of legs	Weakness of both legs; increased deep reflexes; patchy sensory changes with indefinite levels at C 4 and Th 6; multiple telangiectases over body	Negative	Few drops arrested at Th 10	Cohen (3/8/29) Th 10, 11, 12; nevus of cord	Subjective improvement; no objective improvement except that she walked better after 5 months	Received radiotherapy
3	260230	38 M	Sudden while lifting weight	4 months	Progressive	Pain in back; increasing weakness of legs; inability to walk	Weakness of both legs; diminished deep reflexes; sensation diminished below Th 10	.....	.....	Neuhof (11/17/25) Th 7, 8, 9; cord swollen and soft	Postoperative improvement; one year later walked without limp; sensation normal	History of syphilis; Wassermann reaction of blood and cerebrospinal fluid negative; received antisyphilitic treatment
4	271816	42 F	Gradual	3 years	Intermittent; free interval of 2½ years	Weakness of four extremities; stiff neck; diminished sensation in right leg	Weakness of both hands and of left arm and leg; atrophy in both hands; sensory level C 4	.....	No block	Elsberg (10/15/25) C 3, 4, 5, 6; cord appeared smaller and softer than normal	Two and a half years later well and working daily; paresthesias in legs; deep reflexes increased on left	Received radiotherapy
5	272152	50 M	Gradual	6 months	Progressive	Stiffness and shooting pains in both legs; girdle sensation of lower abdomen	Increased deep reflexes; left Babinsky; sensory level Th 8; sweating level Th 6	Negative	.....	Cohen (10/19/26) Th 3, 4, 5; negative	Two years later unchanged	

6	280041	50 F	Sudden	7 years	Intermittent; free interval of one year	Weakness of right leg 7 years, of left leg 6 weeks; inability to walk; temporary loss of sphincter control	Weakness and spasticity of both legs; increased deep reflexes; bilateral Babinski; hyperesthesia Th 3, 4; below this hypesthesia	Negative	Few drops arrested at Th 7, 8	Cohen (6/14/27) Th 6, 7, 8; cord seemed to float on cerebrospinal fluid	No improvement at discharge; no follow-up	Probable multiple sclerosis
7	281289	35 M	Gradual	2½ years	Progressive	Numbness of both legs and feet; inability to walk; dysuria	Paraplegia more on right; deep reflexes absent on right, diminished on left; bilateral Babinski; sensory level Th 10	.....	Reached midsacrum	Cohen (8/15/27) Th 8 and 9 and L 4; apparent widening of canal	Improvement while in hospital died 8 months after discharge	
8	282087	45 M	Sudden; awakened by severe pain	9 weeks	Progressive	Pain in right leg; numbness in right foot	Weakness of right leg; hypesthesia L 5, S 1; tenderness of lumbar and sacral spines	Negative	Part arrested at L 4	Klingenstein (9/16/27) L 3, 4, 5; negative	Improved on discharge; no follow-up	Probably radiculitis
9	286312	31 M	Sudden	14 months	Remission under radiotherapy	Weakness of right leg; dysuria	Weakness of both legs; increased deep reflexes; bilateral Babinski; hyperalgesia at Th 4; below this hypalgesia; indefinite level at Th 4	Negative	Part arrested at Th 4	Cohen (1/6/28) Th 4, 5, 6; negative	Progressive; one year later motor weakness as before; no sensory level	
10	289687	50 M	Gradual	3½ years	Progressive	Weakness and burning in legs; dysuria 1½ years	Weakness of right thigh with atrophy; increased deep reflexes; bilateral Babinski; hypalgesia below Th 4	Negative	Part arrested at Th 4	Cohen (4/8/28) Th 1, 2, 3, 4; negative	One year later improved and working; no subjective complaints; slight weakness on left; indefinite level Th 6	
11	293913	31 M	Sudden after fall	10 months	Progressive	Pain and numbness of right leg; weakness of right leg; girdle sensation in lower abdomen	Spastic gait; weakness of both legs; deep reflexes exaggerated bilateral Babinski; sensory level Th 8	Negative	Few drops Th 3, 4	Cohen (9/11/28) Th 4, 5, 6; cord floated on cerebrospinal fluid	Unimproved at discharge; no follow-up	
12	297431	34 M	Gradual	5 months	Progressive	Weakness of both lower and left upper extremities; dysuria	Spastic gait with out real motor weakness; increased deep reflexes; absent abdominal reflexes; left Babinski; sensory level C 4	Negative	Negative	Cohen (12/14/28) C 3, 4, 5, 6; negative	Five months later improved; weakness of left arm; no sensory, reflex or bladder symptom	

tumor of the spinal cord. Further analysis of these cases shows that with few exceptions the disease from onset to operation has been one of progression starting from a gradual onset. In several instances remissions have been noted. This is rarely found in a tumor, but is not sufficient of itself to rule out such a diagnosis. It should, however, put the examiner on guard lest he should be dealing with a case of multiple sclerosis. In five instances, instead of a gradual onset, the patient fixed the time exactly, and stated that the onset was sudden. This, too, while unusual, may be observed in the case of tumors.

About half the patients noted sensory manifestations as the initial symptom. This took the form of pain or of paresthesia. In only one case did the segment in which the patient complained of pain coincide with the level determined for laminectomy. This was a patient, with pain referred to the back of the neck and the occipital region, on whom a cervical laminectomy was performed. The initial root pains are so important and prominent in most extramedullary tumors that this point is significant. Two patients with girdle sensations in the lower part of the abdomen gave localizing signs in the upper thoracic segments. The paresthesias were referred entirely to the lower extremity; they were described as tingling or burning. In no instance did they extend centrifugally, but always centripetally. Hence they gave no hint that an extramedullary tumor of the spinal cord was not present. Elsberg[4] pointed out that paresthesias extending distally from a proximal point are more frequent in intramedullary involvement. The other half of the patients complained of motor weakness as an initial symptom. This is relatively uncommon in a case of extradural tumor but cannot, of course, rule the latter out.

In no case was a complete spinal block established by manometric determination or by the injection of iodized oil. The latter was used in eight cases. In some instances, a few drops were permanently arrested at the site which clinically was under suspicion. The most suggestive arrest was in the case of neuritis of the cauda equina previously referred to, in which all but a few drops remained at lumbar vertebra 4. In no case at operation was it possible to demonstrate (except in the nevus) the cause for the nondescent of the drops of iodized oil at the level. An arachnoid adhesion which escaped observation is a possible explanation.

In 1912, Bailey and Elsberg,[5] reported improvement in patients showing signs of a level lesion in whom no tumor was found. Such

4. Elsberg, C. A.: Tumors of the Spinal Cord, New York, Paul B. Hoeber, 1925.

5. Bailey, P., and Elsberg, C. A.: Spinal Decompression—Report of Seven Cases, J. A. M. A. **58**:675 (March 9) 1912.

results have been obtained by other observers. In the series reported by Sachs and Glaser, eight of the thirty-three patients were improved following operation. In twenty-four negative explorations detailed by Schönbauer, one fourth of the number showed postoperative improvement. Gordon [6] reported four similar cases.

Reference to the table shows that there is no follow-up record for three of the patients, two of whom were somewhat improved at the time of discharge. Another patient, also somewhat improved, died eight months later of an unknown cause. Of the remaining eight patients, the condition of one was unchanged; one showed progression of the disease; the one who had the nevus was subjectively better but showed no objective improvement, and five were much improved from every standpoint. Of the latter five, one was normal and three were without subjective complaints, but in them some diminution of power with increased reflexes could be demonstrated; the fifth complained of paresthesia in the legs, but she was able to work hard as a domestic.

No satisfactory explanation has been offered for the beneficial effects in the underlying disease, of simple exposure of the cord. In the absence of increased pressure, the term "decompression" has been discarded. Horsley [7] first compared the effect to that seen in celiotomy for tuberculous peritonitis. A change in the local circulation induced by the operation is another theory. That the improvement is fortuitous is not likely; that some patients have spontaneous remissions is true, but it is more than coincidence that in so many cases the improvement begins at the time of operation and seems permanent.

If one could afford to observe over a long period of time a patient with a level lesion, the diagnosis would many times make itself manifest. One would, however, lose the opportunity of obtaining a complete restoration of function if the condition happened to be a tumor. When on one side of the scale is placed the certainty of progression in a case of neoplasm, a progression leading to irreparable damage, and on the other side, the knowledge that simple exploration, properly carried out, should do no harm and may do good even when a remediable lesion is not found, the balance points decisively to exploratory operation.

SUMMARY

A series of twelve cases of nonneoplastic disease of the cord in which laminectomy was done is reviewed.

In eleven cases, the similarity in the onset, course and physical signs to extramedullary tumor is noted.

6. Gordon, W. H.: Laminectomy for Symptoms of Spinal Tumor with Negative Findings, J. Michigan M. Soc. **27**:719, 1928.

7. Horsley, V.: Chronic Spinal Meningitis, Brit. M. J. **1**:513, 1909.

In no case, however, was a complete spinal block demonstrated by manometric tests or by means of iodized oil and the x-rays. Only once was pain referred to the region corresponding to the cord segment involved.

Exploratory laminectomy in doubtful cases is indicated not only to rule out a remediable lesion, but because of the possibility of improvement following the exploration.

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SPECIAL ARTICLE

PROGRESS IN PSYCHIATRY

III. THE SIGNIFICANCE OF KLAGES' SYSTEM FOR PSYCHOPATHOLOGY *

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To trace the evolution of psychiatric thought, both in the past and in statu nascendi, is especially difficult because there are so many indirect extraneous influences from allied sciences. Without a knowledge of such sources the development of psychopathologic ideas and methods cannot be fully understood. In recent years the psychology of Ludwig Klages has exerted an apparent increasing influence on German psychiatry. The appearance of the first English translation of his main work, "The Science of Character," [1] furnishes the occasion for a review of the significance of his system in present day psychopathology.

"The Science of Character" is based on lectures which were delivered between 1905 and 1907. It appeared first in book form in 1910.[2] The fourth edition [3] was considerably enlarged and changed, although the main foundations of the whole system remained the same. Klages' psychologic studies originated in the analysis of handwriting. From the study of graphology, the serious development of which dates back to French authors, notably Michon and Crépieux-Jamin, he came to systematic investigation of character.[4] For a number of years his psychologic writings found little resonance among either psychologists or psychiatrists; but in recent years a number of competent psychiatrists have taken issue with his ideas or have made use of them to a greater or less extent.

* Submitted for publication, Jan. 31, 1930.

1. Klages, Ludwig: The Science of Character, Translated from the Fifth and Sixth German Editions by W. H. Johnston, London, George Allen & Unwin, 1929.

2. Klages, L.: Prinzipien der Charakterologie, Leipzig, Johann Ambrosius Barth, 1910.

3. Klages, L.: Die Grundlagen der Charakterkunde, ed. 4 of Prinzipien der Charakterologie, Leipzig, Johann Ambrosius Barth, 1926.

4. Klages, L.: Handschrift und Charakter, ed. 11 to 13, Leipzig, Johann Ambrosius Barth, 1929; Ausdrucksbewegung und Gestaltungskraft, ed. 3 to 4, Leipzig, John Ambrosius Barth, 1923; Einführung in die Psychologie der Handschrift, Heidelberg, Niels Kampmann, 1928; Zur Ausdruckslehre und Charakterkunde, Heidelberg, Neils Kampmann, 1927; Persönlichkeit. Einführung in die Charakterkunde, Potsdam, Müller & Kiepenheuer, 1929.

To give a brief outline of Klages' study of character is exceedingly difficult. One important principle of his theory of expression is that language itself is an excellent guide to psychology, and that if one takes words that are used in everyday psychology, especially terms of feeling, in their strictly verbal sense, one can make important deductions.[5] He also uses many words in a specific technical sense which is not always self-evident. The terminology is thus difficult to follow, being composed of some words that have to be taken in a definite technical sense, some that have to be taken in a literal sense, and others that have their usual meaning. In giving an account of his system, therefore, one has to guard against the danger either of following him too closely and being too complicated or of reducing his ideas to a too simplified state. Klages' whole psychologic scheme is founded on his own metaphysical ideas. To give an adequate critical estimate of his philosophic background—which cannot be included here—is impossible until the publication of the full systematic statement of his philosophy which he has announced.[6] He is profoundly influenced by Nietzsche [7] and has much in common with Palagyi.[8]

The use of the word "character" by Klages had best be replaced by "personality," for the substance of his study deals with the total personality, while character, in common usage, has a narrower meaning. Klages' chief claim to distinction is that he has outlined the first "complete system" of personality traits. In the characterization of every personality, three "zones" or spheres can be distinguished, each of which has to be viewed with reference to the others and to the whole. In the first place, every person has a certain fund of resources, gifts and capabilities, which serve for the reception, assimilation, elaboration, utilization, preservation and reproduction of mental contents. This Klages calls the "material" of the personality. It includes not only intellectual capacities, but also all sorts of traits formulated with reference to the other aspects of the whole personality. Bleuler [9] denies that Klages' system can be used in psychiatry just because in Klages' conception of the personality, intellectual and affective qualities are combined.

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5. Roback (The Psychology of Character, New York, Harcourt, Brace & Company, 1928) has criticized the emphasis Klages lays on linguistic forms as a source of psychologic conclusions.

6. Klages, L.: Geist und Seele, vol. 1, Leben und Denkvermögen; vol. 2, Die Lehre vom Willen; vol. 3 (in preparation), Die Wirklichkeit der Bilder, Leipzig, Johann Ambrosius Barth, 1929.

7. Klages, L.: Die psychologischen Errungunschaften Nietzsches, Leipzig, Johann Ambrosius Barth, 1926.

8. Palagyi, Melchior: Wahrnehmungslehre, With an Introduction by L. Klages, Leipzig, Johann Ambrosius Barth, 1925.

9. Bleuler, E.: Affektivität, Suggestibilität, Paranoia, ed. 2, Halle, Germany, Carl Marhold, 1926.

This "material" of the personality is arranged in each subject in a specific way, which makes the utilization of all resources conform to an individual pattern manifesting itself in the speed, the choice and the form of the reactions. This part or zone of the person is the "structure" of the personality. According to this structure, the realization of inward tendencies of two different persons, though the tendencies themselves were alike, would show a constant difference in their formal course. The "structure" is especially important for the interhuman relations. One finds here the easy or difficult capacity for stimulation of feelings; capacity for stimulation of will; impulse toward expression and capacity for expression; the fundamental note of life (Lebensgrundstimmung), which varies between expansiveness or the note of life which is keyed high, and "pathos" (passivity), with a note of life which is keyed low. Especial stress is laid on the distinction between capacity for the stimulation of feeling as opposed to capacity for the stimulation of will—that is to say, on the contrast between affectivity and volitional tendencies. Klages finds that general irregularity in handwriting points to a predominance of feeling; general regularity, to a predominance of volition. The actual form of the reaction is determined by the proportion between the strength of the urge and the force of the resistance or inhibition. For example, a "sanguine reaction" may be due either to a strong impelling urge or to a weak inhibiting force.

The third zone is the "quality" of the personality—the individual direction in which the "material" and "structure" find realization according to the personal set of tendencies, urges, instincts and motives. It constitutes a "system of driving forces" which corresponds in a way to the meaning of the word character in a narrower sense.

This is the barest outline of the three "zones" or regions of the personality; namely, the material, the structure and the quality. A few details may be added which, if not illustrative, are at least indicative. Structure is that part of the personality which can be viewed from a quantitative aspect. The first direct standard for the estimation of the capacities of a personality is a second personality. For the estimation of driving forces (motives), however, the standard is a second group of driving forces of the same personality. Klages gives definite formulas expressed in fractions. For example, the capacity for stimulation of feelings (C) grows with the growing liveliness of feelings (L) or diminishes as their depth (D) grows. Therefore the formula is: $C = \frac{L}{D}$.

The fundamental distinction between different personalities is the varying mixture between two fundamental "substances" which exist in

each person; namely, the principles of self-assertion and self-devotion.[10] The driving force of self-assertion has a tendency to the binding of vital processes; the driving force of self-devotion has a tendency to "unbinding" or releasing of vital processes. The driving forces stand to each other in a complicated relationship of polarity which, at least in part, is represented by Klages as quasidynamic in its nature. For example, Klages[1] says: "If I am dominated by an assertive interest, then it dominates, among other things, a possible tendency to devotion, and accordingly every stimulus to devotion is felt as an irritant serving to intensify the assertive interest. If, conversely, I am dominated by a tendency toward devotion, then it also dominates my assertive interest and my strongest reluctance will be turned against assertive desires; the assertive functions of my will (which, of course, are indispensable) serve merely the realization of such ends as satisfy desires of devotion."

Outlining a "system of driving forces" (interests), Klages arrives, according to his dichotomy, at the following scheme:

Releases[11] *(Release of Vital Force)*	*Bonds*[12] *(Binding of Vital Force)*
Self-devotion	Self-assertion
Capacity for enthusiasm	Reason
Depth of feeling (capacity for passion)	Egoism (selfishness)
Fundamental note of life: passivity, belief in the past, reverence	Fundamental note of life: activity, belief in the future, will to seize (utilitarianism)
Opposing poles of mood: melancholia—serenity	Opposing poles of mood: pleasure from success (euphoria)—displeasure from failure (dejection)
Opposing poles of self-estimation: pride—humility	Opposing poles of self-estimation: self-esteem—self-doubt
Fundamental conviction: a world of animate phenomena (which happen and cannot be possessed)	Fundamental conviction: a world of facts (which can be seized and held)

Within this scheme a large number of mental tendencies, such as benevolence, faithfulness, patience, suspicion, hypocrisy, love of intrigue and intolerance, are enumerated, all neatly classified on the left or right side of the scheme.

Within the "quality" of the personality the distinction between instincts and conscious will is especially emphasized.[13] Will corresponds to self-assertion, reason and egoism; the instinctive life to self-devotion,

10. This distinction corresponds to a distinction between spirit and soul, the former the male, the latter the female element. Klages points to the analogy of gender in the Greek word for spirit (ὁ νοῦς) and that for soul (ἡ ψυχή).

11. In German: lösende Antriebe.

12. In German: bindende Antriebe.

13. Klages, L.: Die Triebe und der Wille, Arch. f. Psychiat. **85**:478, 1928; Zur Theorie und Symptomatologie des Willens. Pamphlet.

enthusiasm and passionateness. Will does not cause movement; it is an inhibiting force. To will means that something should not happen; namely, all that which might distract from the direction of the goal. In volition there is always a subjective element of activity, of self-assertion, of consciousness; in all other instinctive tendencies, a subjective element of passivity and laissez faire. The will is in a way opposed to the whole material of the personality whence it originates. It can direct it but cannot fundamentally change it.

Klages has touched on a number of psychopathologic problems in his writings. Manic-depressive psychosis is primarily a disease of the "structure" of the personality. The two phases of this condition can be explained by contrasts in the personal capacity for stimulation of the will. This capacity results from the habitual proportion between the moving forces and the inhibitive tendencies. In manic states there is a decrease or lack of inhibiting forces, as evidenced by the fact that the processes of association are slower, despite the tendency to hyperactivity. In depression, on the other hand, there is a paralysis of the moving forces.

More interesting than this formal and cursory reference to affective psychoses is his conception of the hysterical character. This is characterized, he says, by the disproportion between abnormally decreased capacity for expression and highly developed impulse toward expression. "The hysterical organism in its logical perfection and in its highest (and practically impossible) intensity would be a reflector reflecting external light only, presenting the image of a mock-life by means of organic imitation of alien lives. There is certainly a wide difference between the servant girl who, without knowing it, acquires the symptoms of the disease of the child whose nurse she is, and a Veronica Giuliana, who in a state of convulsions receives full stigmatization; still they agree on one point—with all their symptoms they merely repeat external impressions. Imitation is the common characteristic of all hysterical phenomena." [1]

In a recent paper, Klages [14] has developed a concept of psychopathic personalities which, though certainly not valid for this whole group, may be helpful for the understanding of certain small groups of personalities. He emphasizes an ingrained tendency toward self-deception. There is a great contrast in the individual's life between the actual truth and appearances. But appearances are believed in, and have to be believed in, almost as a necessary condition for the very continuation of life. This is again a formal characterization, which leads Klages, not surprisingly, to a denial that therapy is of any help here.

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14. Klages, L.: Bemerkungen zur sogenannten Psychopathie, Nervenarzt **1**:201, 1928.

Various aspects of Klages' work exert an influence on present-day psychopathology. It is indeed surprising how many psychiatrists have in recent years absorbed parts of Klages' teaching. The most complete plea for making Klages' outline of personality the basis of the study of major and minor personality disorders is made by Kehrer.[15] His ideas may therefore be briefly sketched. The many-sidedness of Klages' outline, including as it does not only "school psychology" but also those phenomena which scientific psychology so frequently neglects, appeals to him especially. He points out that within the "quality" of the personality there is a place for dynamic conceptions such as the libido of psychoanalysis. The "material" of the personality is that which formed the substructure of Wernicke's psychiatry and which is affected in the different forms of organic dementia—in contrast to catatonic dementia, in which the "material" of the personality is intact while the other two "zones" of the personality suffer. The growth and development of the personality is determined by the system of driving forces (interests) in contrast to the relative rigidity of the structure of the personality which is usually only quantitatively modified by outside influences or occurrences. Structure therefore corresponds to constitutional disposition and to a cross-section—quality to developmental tendency or to a longitudinal section. Kehrer proposes a hierarchy with the three different "zones" at different levels. The "quality" is the most important zone. The key to the understanding of personality disorders lies in conflicts of antagonistic parts within the quality zone of the personality, not in the temperament or the associative capacity of the subject (structure or material). According to Kehrer, the three zones of the personality have an important dynamic relationship to each other. In manic-depressive psychosis, for example, the structural part of the personality is primarily affected, but secondarily the other zones are also involved. The character of the personality in the narrower sense, that is the quality in the sense of Klages, is not in a state of conflict; it is syntonic (Bleuler) within itself and syntonic —that is harmonious—with the other two zones; namely, with the structure and material. Cycloid and schizoid reactions are due to different shunts between quality and structure (character and temperament). The quality is the nucleus or higher level of the personality. Disorders of structure and material with intact quality are possible, but not disorders of quality with intact structure and material. Hysteria, obsessive neurosis, delusional disorders, psychopathic personalities—all have their seat in this quality zone of the personality.

15. Kehrer, F., and Kretschmer, E.: Die Veranlagung zu seelischen Störungen, Berlin, Julius Springer, 1924.

To a far less degree, other authors have accepted Klages' system. His distinction of three zones within the personality and the main characterizations of the three zones have been accepted by Kronfeld,[16] Schultz,[17] Schneider,[18] and various others. Hoffmann,[19] in his survey of problems of character formation, devoted a section to Klages. Ewald [20] has evidently been influenced by Klages' discussions of temperament, and has evolved a theory of the relation between personality and psychosis which has points of contact with Klages' views. Attempts to use Klages' scheme of personality traits clinically have been made by Lange [21] for paranoiac psychoses and by Homburger [22] and Voigtländer [23] for children with behavior disorders. Part of Klages' formulation of hysteria has been accepted by Kahn.[24] Jaspers [25] in his book on general psychopathology presented Klages' system as one of the most important attempts at personality analysis, while Prinzhorn [26] has recently made Klages' teaching practically the basis of a presentation of psychotherapy. Reichardt [27] stated the belief that Klages' sharp distinctions between instincts, driving forces and the conscious will are an important consideration for the understanding of somatopsychic relationships. Langeläddeke [28] has made interesting experiments on rhythmic expression in healthy and in mentally diseased persons, in the interpretation of which he has made use of part of Klages' theories of expression. He found deviations of rhythm in schizophrenic patients which he considers as mild catatonic motor phenomena.

16. Kronfeld, Arthur: Psychotherapie, ed. 2, Berlin, Julius Springer, 1925.

17. Schultz, J. H.: Die konstitutionelle Nervosität, in Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1928, vol. 5.

18. Schneider, Kurt: Die psychopathischen Persönlichkeiten, Leipzig, Franz Deuticke, 1928.

19. Hoffmann, Hermann: Das Problem des Charakteraufbaus, Berlin, Julius Springer, 1926.

20. Ewald, G.: Temperament und Charakter, Berlin, Julius Springer, 1924.

21. Lange, J.: Ueber die Paranoia und die paranoische Veranlagung, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:85, 1925.

22. Homburger, A.: Psychopathologie des Kindesalters, Berlin, Julius Springer, 1926.

23. Gregor, A., and Voigtländer, E.: Die Verwahrlosung, Berlin, S. Karger, 1918.

24. Kahn, Eugen: Die psychopathischen Persönlichkeiten, in Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1928, vol. 5.

25. Jaspers, Karl: Allgemeine Psychopathologie, ed. 3, Berlin, Julius Springer, 1923.

26. Prinzhorn, H.: Psychotherapie: Voraussetzungen, Wesen, Grenzen: Ein Versuch zur Klärung der Grundlagen, Leipzig, Georg Thieme, 1929; Die Begründung einer reinen Charakterologie durch Ludwig Klages, Jahrb. d. Charakterol. **4**:115, 1927.

27. Reichardt, Martin: Brain and Psyche, J. Nerv. & Ment. Dis. **70**:390, 1929.

28. Langelüddeke, A.: Rhythmus und Takt bei Gesunden und Geisteskranken, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:1, 1928.

A popular exposition of the "science of character" according to Klages was given by Hermann [29] as early as 1920. His book attempts to apply the subject to problems of education and mental hygiene in general. It is perhaps the best brief introduction to Klages and is free from metaphysical discussions.

There is little doubt that in scientific psychiatry Klages' system as a whole cannot and need not be absorbed. In reading his writings one is surprised how many traits and qualities it is possible to group in various combinations without the emergence of any lifelike human personalities. It is a psychology which, to formulate a personal impression, deals with the shadows of persons rather than with the persons themselves. This is partly due to Klages' neglect of genetic-dynamic principles, especially the dynamic values of the mental contents of psychic life. The criticism must be made, in regard to his treatment of instinctive tendencies, that he neglects psychosexual phenomena.

But Klages' books contain many bright flashes. These consist not only in stimulating ideas, but also in good psychologic observations which cannot be found elsewhere. His reliance on the verbal significance of linguistic designations is interesting and suggestive of psychoanalytic tendencies, although he rejects psychoanalysis completely. The broad outline of his division of the personality undoubtedly has its usefulness. His main significance, however, lies in the fact that he has drawn attention to a more intricate complexity of personal traits than psychopathology usually considers. It will be interesting to observe to what extent and with what results his ideas will continue to be absorbed in psychopathology.

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29. Hermann, O.: Dr. Klages' Entwurf einer Charakterkunde. Für Erzieher allgemeinverständlich besprochen und auf die Heilpädagogik angewandt, Leipzig, Johann Ambrosius Barth, 1920.

News and Comment

FELLOWSHIP IN PSYCHIATRY

The Institute for Child Guidance, established and maintained by the Commonwealth Fund in New York, offers one-year fellowships to properly qualified psychiatrists desiring to enter the child guidance field and wishing to work in organized clinics. Ordinarily three fellowships in psychiatry are available in the spring (May 1 or June 1) and three in the fall (September 1), the annual total being six. Applications will be received at any time throughout the year. Appointments are based on the record of the applicant, reports from those given as references, and personal interviews with the committee on award. The applicant must be not more than 35 years of age; a resident of the United States; must possess the M.D. degree from a Class A medical school; should, preferably, have had an internship in a general hospital, and must be adequately grounded in the fundamentals of psychiatry; by this is meant sufficient experience on an active clinical service dealing with the problems of formal psychiatry in a hospital in which the training of psychiatrists is a definite part of the program. The time required is about two years, during which by reading, staff conferences, etc., the material acquired in actual contact with the patients is adequately digested and interpreted. For further details or for application forms, address Lawson G. Lowrey, M.D., Director, Institute for Child Guidance, 145 East 57th Street, New York.

Abstracts from Current Literature

HEADACHES IN OTO-NEURO-OPHTHALMOLOGY. (PHYSIOLOGY, PATHOLOGY AND TREATMENT.) HALPHEN, MONBRUN and TOURNAY, Rev. d'oto-neuro-opht. **7**:161 (March) 1929.

This comprehensive article fills the entire number of the journal. It is divided into three parts and an introduction. In the introduction, headaches are classified and the sensory innervation of the head is described. In part 1, the sources of headache and their manner of occurring is discussed; part 2 is devoted to an explanation of the mechanism of their development, and in part 3, the treatment is detailed.

Headaches are classified as simple pain in the head; cephalalgia, used to describe a more pronounced type, and migraine. The particular kind of headaches discussed in this article are those pains, slight or severe, intermittent or continuous, prolonged and obstinate which justify special ophthalmologic, otorhinologic or neurologic examinations in order to institute a rational therapy. The fields of reception and projection of head pains are found, inside or outside the skull, in that complex innervation where the distribution of the cerebrospinal system is intermingled with that of the sympathetic and parasympathetic systems.

External cranial innervation takes place both by cranial and spinal nerves, the trifacial and the occipital; the sympathetic and parasympathetic fibers are carried with the arterial arborizations. The limits of innervation are not absolutely fixed and there is free anastomosis of the terminal fibers. The perivascular plexuses come from the cervical sympathetic fibers and accompany the internal carotid artery and the external carotid as far as the occipital artery. It is probable that the parasympathetic fibers also reach these vessels by means of the posterior spinal roots and certain cranial nerves.

In endocranial innervation the cerebrospinal contingent is almost entirely furnished by the fifth cranial nerve, which supplies the dura, the walls of the venous sinuses and the bones. A small area in the region of the posterior lacerated foramen and of the lateral sinus is innervated by a meningeal branch from the jugular ganglion of the vagus. Fibers from the gasserian ganglion supply the adjacent dura and the superior petrosal sinus; the ophthalmic division gives fibers to the cavernous sinus, the fronto-orbital dura and, through the recurrent nerve of Arnold, to the tentorium. The superior maxillary division, through the recurrent nerve of Schwalbe, innervates the dura of the anterior surface of the petrous and of the parietal bones; from the inferior maxillary division the recurrent nerve of Luschka, reenforced by a branch from the otic ganglion, is distributed to the mastoid cells and the temporoparietal region. The cerebellar fossa and the occipital sinus are supplied by a small group of fibers which the hypoglossal "borrows from the trifacial by an anastomosis coming from the lingual."

Sympathetic and parasympathetic fibers supply the pia and its vessels, certain regions, as the base and the choroidal plexuses, being more richly endowed. The vessels are innervated by parasympathetic fibers from several cranial nerves and by sympathetic fibers from the carotid and vertebral plexuses. The nerve terminations in the pia are considered sensory receptors; the question is more complex in regard to the vessels, although it may be assumed that sensory receptors are intermingled with the vasomotor fibers.

This complex innervation of the exterior and interior of the skull is in close connection with the innervation of the nose and eye, through the fifth nerve and the perivascular plexuses. In addition to the anterior and superior walls of the external auditory canal, the anterior part of the ear drum, the mucosa of the mouth, tongue and soft palate, the trifacial is distributed to the entire nasal fossae

back to the free edge of the palate and the pharyngeal orifices of the eustachian tubes, as well as to the orbits and their contents. Its various branches traverse foramina or canals in the skull and are thus in contact with unyielding surfaces.

After describing the course and distribution of the branches of the ophthalmic division, attention is drawn to the rich association of the sympathetic and parasympathetic systems. Sympathetic fibers arise from the superior cervical ganglion and accompany the vessels as the carotid and cavernous plexuses supplying the ophthalmic ganglion. The long ciliary nerves go directly to the ocular bulb and are the dilators of the pupil; the short ciliary nerves belong to the parasympathetic system and are the postganglionic fibers of the ophthalmic ganglion, which innervate the constrictors of the pupil. Another parasympathetic supply issues from the bulb with the facial and reaches the sphenopalatine ganglion by the vidian nerve; from the ganglion, postganglionic fibers reach the lacrimal gland via the superior maxillary nerve and the orbitolacrimal loop.

In the domain of rhinology, similar complexity is met through an intermixture of the parasympathetic and sympathetic fibers with the trigeminal distribution. The nasal branch of the ophthalmic supplies the sphenoidal and posterior ethmoidal sinuses, the superior part of the nasal septum, the heads of the turbinates and the lobule of the nose. The frontal branch innervates the frontal sinus. The second division of the trigeminus in the skull lies in a small canal in the great wing of the sphenoid and could be compressed by an alar extension of the sphenoidal sinus. In the passage of this part of the trigeminus through the foramen rotundum, the posterior ethmoidal cells are in relation with it. It then enters the pterygomaxillary fossa, proceeds through the sphenomaxillary fissure and infra-orbital canal to the surface of the upper jaw. If there is a dehiscence in the lower wall of the canal, it is separated from the antrum only by mucosa. The situation of this nerve in bony canals or along rigid surfaces makes it susceptible to pressure from swelling, and this is true of almost all of its branches.

The mandibular branch leaves the skull through a large opening, the foramen ovale, and is accompanied by a venous network which unites the pterygoid and cavernous plexuses. The sympathetic supply is from the carotid and cavernous plexuses, which accompany the vessels, and also from the sympathetic roots of the three ganglia, ophthalmic, sphenopalatine and otic.

The parasympathetic supply reaches the ganglia by means of their motor roots. Thus the vidian nerve, formed by the superficial petrosal from the facial and the deep petrosal from the glossopharyngeal and by the sympathetic root, reaches the ganglion after traversing the vidian canal. Fibers go from the ganglion to the superior maxillary division and thus supply the whole nasal fossa.

This rich distribution of the sympathetic and parasympathetic fibers with the fibers of the trigeminus is of capital importance in understanding the pathologic physiology.

Experiments on animals and observations on man have established the fact that there is sensitiveness of different layers of the interior and exterior of the skull and have given glimpses of certain mechanisms in the production of headache. Various parts of the head have varying degrees of sensibility. Thus, the small nervous trunks in the scalp, and especially the aponeurosis, are particularly sensitive, while the bone is little so. The dura itself is sensitive, especially in the regions of the nerve trunks and the arteries, while the brain tissue has no sensation to pain.

The injection of air into the ventricles and the blocking of the return circulation from the head, as in the procedures of Queckenstedt and Bier, cause headache.

Cushing noted dilatation of the retinal vessels on using the cuff of a blood pressure apparatus around the neck when the pressure equaled 80 mm. of mercury, and Forbes, Cobb and Fremont-Smith observed dilatation of the retinal veins and hyperemia of the papillae after inhalation of carbon dioxide for half an hour.

PART 1.—SOURCES AND ACTIVATION OF HEADACHES.—1. *Ophthalmology:* A. Sources. It is necessary to make a complete objective and functional ophthalmologic examination in the majority of cases of headache. This must include an

examination of the fundus, a testing of the oculomotor functions and visual fields, and an estimation of central vision after having determined the refraction. The results, positive and negative, will indicate whether the ophthalmic manifestations are part of an endocranial or other syndrome or whether they are purely ophthalmologic.

The "irritative points" in the setting up of headaches in the domain of ophthalmology are diseases of the orbit, the eye and their sensory pathways, and errors of refraction. Pathologic conditions of the orbit include: tumor, traumatism, osteoperiostitis (especially syphilitic periostitis) and such inflammations as tenonitis, orbital cellulitis and phlegmon and complications of sinusitis. Inflammations of the globe cause pain which may be localized in the eye but is often radiated to the vertex, temples, mastoids or occiput. Pneumococcic ulcer of the cornea is often the cause of head pain. Scleritis and episcleritis, especially the rheumatic forms, produce obstinate headache, often marked at night. Iritis, iridocyclitis and panophthalmia cause violent headaches with concomitant intra-ocular hypertension. Rarely do lesions of the choroid and retina cause headaches, although Morax has noted deep orbital pain in chronic syphilitic chorioretinitis. The most excruciating headaches accompany acute glaucoma: they are especially marked in the forehead, temples, vertex and neck, and are associated with vomiting during the crises.

Among the neuralgias are mentioned those which complicate paralysis of the third cranial nerves (part of the syndrome of ophthalmoplegic migraine) and those symptomatic of a neoplasm, or tuberculous or syphilitic lesion situated in the course of the ophthalmic nerve or at the gasserian ganglion.

As regards the sympathetic, Monbrun and Benisty have described a syndrome "causalgique" following wounds of the eye. The pains develop several months after the injury, are continuous, hemifacial and hemicranial or even bilateral. Especially important is the radiation to the vertex. At this point there is a sensation of pricking, like an electric current. Accompanying it, there is a sensation of painful movements of the interior at the lower part of the thorax and the epigastric notch. These patients have a sensation of being burned by a red hot iron; the skin becomes purple and drops of sweat stand out on the face during the crises.

Errors of refraction are often the cause of headache. Hypermetropia is the one most often overlooked and is the most common offender. Asthenopia develops if the close work is prolonged.

Among the vasomotor signs is hyperemia of the fundus (not to be confused with stasis). If astigmatism is present with hypermetropia the preceding signs are intensified but, on the contrary, they are less marked in the association of astigmatism and myopia. Presbyopia supervening on hypermetropia intensifies the headaches. Anisometropia or anything interfering with good binocular vision and convergence is often a source of headaches.

B. Mechanism of the production of headache. In ocular headaches, more and more complex mechanisms are encountered as one proceeds from the consideration of tumor or inflammation of the orbit as a source, to the study of errors of refraction. In the former, the direct effect of pressure on the sensitive pathways is sufficient to cause the pain. This is also true of inflammations of the globe, but in addition to the orbital innervation, the globe is controlled by the ciliary nerves and the ophthalmic ganglion, which are motor, sensory and vasomotor organs, belonging to both the sympathetic and cerebrospinal systems. The eyeball is a closed cavity, rich in vascular plexuses, and therefore variations in ocular tension occur easily in inflammatory conditions.

Like intracranial tension, ocular tonus requires an efficient regulator to afford protection for the delicate retinal elements and to maintain proper pressure for the visual function under the varying conditions of atmospheric and blood pressure, and the movements of the eye, pupil and lens. The innervation which regulates ocular tension is in close relation with distant organs, a fact that is illustrated by the phenomenon of the oculocardiac reflex. Variations in ocular tension produce distant reactions as, for instance, the violent headaches and vomiting in acute

hypertension and the violent occipital headache in sudden hypotension from traumatism or surgery on the globe.

As regards the "irritative points" in the sympathetic system, Head has shown that intra-ocular conditions are in relation with hyperalgesic zones in the vertex, forehead and temples. They are associated with the medullary elements of the fifth to eighth thoracic segments which, themselves, are in relation with the sympathetic innervation of the viscera of the inferior thorax and upper part of the abdomen.

As to alterations in the sensory pathways of the visual apparatus, no explanation is needed of headaches caused by tuberculous, syphilitic or other troubles affecting the ophthalmic branch of the gasserian ganglion.

The importance of the sympathetic in painful manifestations of ocular origin is shown by the occurrence of neuritis of the sympathetic ("syndrome causalgique" of Monbrun and Mme. Benisty). In addition to the classic symptoms of pain, vasomotor and secretory disturbances, there occur mental aberrations (suicidal attempts), radiation of pain to the vertex and epigastrium, disappearance of the syndrome after orbital injection of procaine hydrochloride, and appearance of the syndrome in spite of anesthesia in the whole domain of the trigeminal.

The sympathetic is undoubtedly involved in the mechanism of the obstinate neuralgias and headaches in zona ophthalmica and in certain neuroparalytic keratitides. The fact that the use of short applications of medical diathermy causes rapid disappearance of certain objective signs and of obstinate headache in cases of zona and of neuroparalytic keratitis points to a vasomotor mechanism in the production of this symptom. Two illustrative case histories follow.

A short résumé of the mechanics of normal binocular vision, explaining the necessary, perfect coordination of the muscles of the eye, head and neck, precedes the discussion. The diagnosis of headache due to hypermetropia presents the most difficulty in those who have an error of only 1 or 2 diopters, and in the child who, in spite of hypermetropia, bends over his work and maintains a condition of spasm of the ciliary muscles. The last can easily be mistaken for a myope unless his accommodation is paralyzed by atropine before refraction. The slightly hypermetropic person gets along well until he approaches the period of presbyopia. Then his effort at accommodation proves too great and headache supervenes. This same thing happens to the person during pregnancy, convalescence or prolonged fatigue. When a person with a hypermetropia of 2 diopters looks to a distance, instead of making no accommodative effort, he constantly makes an effort of 2 diopters, and the convergence associated with this effort corresponds to nothing since the optic axes must remain parallel. When he looks at a distance of 33 cm., he must make an effort of accommodation of 3 diopters, plus 2 more to compensate for his hypermetropia — 5 diopters in all. But, still more important, this excess effort calls forth too much convergence, and diplopia is produced with its attendant ills. Thus the complex muscular harmony of binocular vision is broken. This muscular discord causes not only headache but also objective troubles — congestion, red lids and hyperemia of the disk.

Myopia is more rarely a cause of headaches. There is here too a discord between accommodation and convergence, but it is not regulated by an effort as in hypermetropia. Astigmatism with hypermetropia causes the most typical and intense headaches, associated with vasomotor disturbances.

In anisometropia it is evident that the lack of equilibrium between accommodation and convergence, present in hypermetropia, is even more marked. Correction of the error is difficult because of amblyopia in one eye from lack of use, which is sometimes present.

In presbyopia, the troubles arising are of the same order as those in hypermetropia and are often added to the latter.

2. *Rhinology:* Direct attack on the nerve terminations is found in all hypertrophies in the nose, in tumors, polyps, syphilis, etc. The pain, however, can be due to radiations made on the spot or to reflex action. The principle is expressed that, in indirect headaches, a single pathogeny can be proved only where the fibers

of the trigeminus and the sympathetic are intimately intermixed. The nerves and blood vessels go through bony canals before penetrating the mucosa and their proximity to the nerve centers is close.

More complex reflexes, not systematized to one nerve distribution, suggest a sympathetic mechanism.

A. Endonasal sources of headache: The head discomfort from acute coryza is attributed to obstruction due to vasomotor derangement. Nasal obstruction can be caused by numerous conditions which themselves are only a part of the clinical picture and the diagnosis is easily made. The most frequent mechanism of sensory disturbances of nasal origin is compression of the nerves by osseous pressure or neuritis.

B. Origin from nasal sinuses: The picture of acute frontomaxillary sinusitis is described and the point is made that this headache is a neuralgia due to retention of pus.

The painful catarrhs, described by Luc, occur mostly in women and are characterized by periodicity of the pain, tenderness and absence of secretion in the nose. Luc attributes them to narrowness of the infundibulum. Closely akin to this is the "vacuum sinus" of Sluder, due to closure of the infundibulum by an enlarged middle turbinate. The authors reject the explanations of both Luc and Sluder. Headache from ethmoiditis is due to neuralgia and not to retention of secretion.

In sphenoidal sinusitis, the headache is deep seated, occipital or parietal, and radiates toward the shoulders and arms, ears and mastoids. The eyes seem to be drawn into the orbits or pushed forward. The head feels as if it were in a vise, and there are paroxysms of pain, exaggerated by reading or intellectual activity. There is sometimes vertigo, nasal obstruction and pharyngeal secretion. Frequent colds occur. The headache does not have the neuralgic character of pain due to obstruction of the nasofrontal duct; it is continuous with exacerbations, is especially marked at night and lasts for years. It is relieved by catheterizing the ostium, opening the cavity or cocainizing the interior. Sluder and Wright, Liébault, Alden and others have accounted for this syndrome in various ways, but one may recall the facts that the superior maxillary nerve is in a close relationship with the cavity, and that the vidian nerve runs in a canal in the wall of the sinus. Neuralgia can be caused by compression of the nerves in their canals and by disease of the canals themselves, and the pain may be propagated to all the constituent branches: to the mastoid and auricle through the petrous fibers from the facial, to the cervical and pharyngeal regions through the deep petrosal and the glossopharyngeal by the nerve of Jacobson and its intermediary.

Headaches of more complex mechanism, meatal headaches, headaches without lesions and causalgia: Most patients with headaches, the origin of which has not been discovered and which have not yielded to treatment, have no nasal or sinus lesion. Although the pain is localized over one or another sinus region and there may be present a unilateral mucoid or purulent secretion, all rhinologic examinations show the integrity of the nose and adnexa. Nevertheless, the origin of the headache is endonasal and an anesthesia of the trigeminosympathetic fibers cures the algias. Such patients are usually women, and their pains are continuous but subject to exacerbations which arise always from the same causes: the menstrual period or the days which precede or follow it, lying down, the warmth of the bed, passing from warmth to cold as on getting out of bed in the morning, and emotional shock. The beginning of the trouble is often a nasal condition, sinusitis, grip, etc. The pain may be at the root of the nose, over Ewing's point, orbital, periorbital or retro-orbital and efforts of accommodation increase it. There may be either exophthalmia or enophthalmia. The temples feel as though they were constricted in a vise; the scalp is hypersensitive, the neck, mastoid and ear are sensitive. Or the radiations may go to the shoulders, back teeth, palate or larynx (clearing the throat, cough). There is smarting in the nose and soft palate, tickling which causes sneezing, tingling in the cheek like the trickling of water. There may be a little snuffling, a sense of obstruction in the nose or spasmodic rhinitis with sneezing and hydrorrhea which may become purulent.

On the other hand, there may be no endonasal symptom other than pain. Examination reveals a narrowness of the upper part of the olfactory slit due to deviation of the septum or hypertrophy of the middle turbinate or a spur piercing the turbinate. If a cotton-wound applicator is forced between the septum and turbinate it causes violent pain and a slight hemorrhage. Cocainizing this area relieves the patient's suffering almost immediately. The cause is compression in the narrow defile of the superior meatus of the fibers from the trigeminus or sphenopalatine ganglion.

Sphenopalatine neuralgia, described by Sluder in America, and Ramadier, Sargnon, Terracol and Halphen in France, is a sympathetic headache, a veritable nasal causalgia. Anesthetizing the ganglion often brings relief. Not all persons who have an obstruction to the free circulation of air or blood in the upper posterior part of the nose suffer from this syndrome. There must exist a groundwork of hyperexcitability or disequilibrium of the sympathetic system. These patients are neurasthenic. Their symptoms are described in great detail. The least emotion awakens the pain; medicines, as cocaine, are badly borne, causing chilliness, sweats, tachycardia and psychic excitation even from small doses.

Study of the nasofacial reflex will furnish proof of the diagnosis. An irritant or caustic application to the upper posterior part of the nose quickly causes tearing, nasal hydrorrhea, congestion of the conjunctiva and skin of the face and neck. Endocrine disturbances play a large rôle in these headaches. The menstrual period brings on crises and pregnancy makes them disappear; there is constant fatigue, physical and moral depression suggesting suprarenal dysfunction.

3. *Headaches in Neurology:* 1. Exocranial sources. Traumatisms, local hemorrhage and infections, erysipelas and zona as a cause of headache are not considered. Cephalalgias of muscular and inflammatory origin cause extensive and protracted headaches. They are characterized by infiltrations in the muscles of the head and neck, at first edematous and then more dense, which are palpable and painful to pressure. They act by irritating the nervous elements.

2. Cranial sources are represented by osteitis, caries, exostoses and neoplasms.

3. Endocranial sources. The true endocranial headaches are engendered in the most recognizable way by those processes which are in conformity with palpable changes of the central nervous system and its coverings. Tumors and meningitis are the most striking examples. Tumors cause headaches directly both by interference with the equilibrium between production and resorption of the cerebrospinal fluid and by an increase of the volume of the cranial contents. Tuberculosis, syphilis, abscess or infectious processes can behave like tumors. Headaches following concussion or trephining are due to small intracranial lesions and cicatrices but are most often the result of changes in pressure of the cerebrospinal fluid. Both hypertension and hypotension are sources of headaches. In the latter, spinal puncture increases the pain. Epileptic headaches are due to interference with the cerebrospinal circulation with disturbances in the vascular and sympathetic systems. A warning is given against attributing to vascular spasm all encephalic processes.

The headaches of meningitis are due to changes in intracranial pressure and are ameliorated by spinal puncture. The questions of headaches from ossification of the meninges is not settled. In epidemic encephalitis and multiple sclerosis, the headaches are due to involvement of the meninges and the nerve centers.

Characteristic headaches accompany cerebromeningeal syphilis. In the secondary stage, the cause of the headache is probably disturbances of the function of the vegetative system by the syphilitic infection.

4. *Apparently Distant Sources:* Evidence is introduced which tends to prove that headache from sources distant from the head is due to changes in pressure of the spinal fluid; asphyxia from inhalation of carbon monoxide, lead poisoning, uremia, gout, diabetes and sunstroke. The explanation is not so simple in cardiovascular headaches, in which biochemical factors intervene.

The neurovegetative system participates in the production of migraine or visceral headaches due to conditions of the stomach, intestines and gallbladder. Direct or indirect disorders of the sympathetic nervous system have been noted in explaining the pathologic physiology of headaches. Barré has described a posterior cervical sympathetic syndrome related to such disorders of the cervical region as chronic vertebral arthritis.

PART 2.—EXPLANATION OF THE MECHANISM.—1. *Direct Action:* The sensory nerves may be directly affected at various parts of their course by harmful processes, either mechanical or toxic irritations. Thus they may be compressed in the rigid walls of their bony canals, the so-called "nevrodocites." This same direct mechanism is seen in endocranial headaches when changes in pressure of the fluid come into play.

2. *Indirect Action:* The reflex pain from a diseased tooth may extend to other teeth and even to the cheek and to the skin. This reflex may take a short direct pathway or, on the other hand, the course may be long and complex. Thus Mairet and Piéron found cases of concussion in which pressure on the supra-orbital caused pain in the occipital nerve distribution and vice versa; in one case, the destruction of the supra-orbital branch did not abolish this reflex; the explanation is that the transmission is through sympathetic conductors.

3. *Projection Visceral Algias:* Dejerine has pictured certain cutaneous hyperalgesic zones of the head in relation with certain root segments of the cord and their corresponding visceral relations. For example, the frontonasal zone is related to the third and fourth cervical, the midorbital zone to the second and third dorsal. Daniélopolu has succeeded in abolishing these hyperalgesic zones by anesthetizing the appropriate nerve trunk.

4. *Causalgia:* This syndrome differs from the sensitive and painful symptoms accompanying ordinary neuralgia and neuritis. It produces a sensation of burning like a mustard plaster, which varies in intensity from a feeling of warmth to a torturing pain, described by Weir Mitchell. The participation of the sympathetic has been suspected by all observers. The painful phenomena are accompanied by changes in circulation, temperature and secretion. It is important to note that these troubles follow almost exclusively wounds of the median and sciatic nerves which receive at their origin a large sympathetic supply and enjoy an exceptional vascularity.

The participation of the sympathetic in the regulation of sensibility has been shown by experimentation.

Claude Bernard, in 1851, noted that, after extirpation of the superior cervical ganglion in a cat, the sensibility of the corresponding side of the face was augmented. He also found that during fasting it was possible to irritate the pneumogastric without producing the least pain, while during digestion the least irritation produced evidences of painful sensations in the animal. There exist, then, physiologic variations of sensibility whose cause is to be found not in the brain but in the periphery of the nerve. In the stomach one sees the mucosa become red and tumefied on contact with food while it is pale and bloodless when the stomach is empty.

5. *Disturbances of Intracranial Pressure:* The mechanisms just described can easily be transposed from the limbs and visceral cavities to the exterior and interior of the skull in order to explain some headaches. But another factor is the disturbance of endocranial equilibrium. The soft brain, lying in a rigid osseous box and subjected to humoral and biochemical changes, is provided with a rich blood supply; it is surrounded by the pia, also rich in blood vessels, and lies on a bed of liquid, the cerebrospinal fluid. Changes in volume of cerebral contents can be quickly compensated by compressible masses of fat and venous plexuses lying outside of the spinal dura. These venous plexuses can quickly empty into the extraspinal plexuses. The spinal fluid itself can vary in quantity, as can also the mass of blood in the cranium, as well as the brain itself according to its liquid content. A state of equilibrium is maintained by a counterbalancing of

all these factors, probably through a nervous mechanism. Forbes and Wolff have shown that the pial circulation is under control of the vasomotor nerves and that the introduction of hypertonic solutions causes a visible constriction of the sanguineous network in the pia. Kubie and Hetler photographed this constriction of the pial vessels and found also a reddening of the cortex itself. On the other hand, by introducing distilled water, they obtained and photographed a blanching of the cortex between the dilated pial blood vessels.

It is supposed that the nerve terminations, both vasomotor and central, in the pia and choroidal plexuses take part in regulating the spinal fluid circulation. It is a delicately balanced mechanism and keeps the total endocranial volume constant. It is easily understood that interference with this delicate mechanism by changes in circulation, blockage in the cerebrospinal circulation, and pathologic processes, as hemorrhage, neoplasm, etc., can result in headaches. Increase in endocranial pressure is a most frequent cause of headaches.

Hypotension headaches are also found following spinal puncture. It has been shown that, following this procedure, there is a leaking of fluid through the gaping needle wound in the dura for some time afterward. In the case of hypertension the sensory nerve fibers are compressed by the mass of fluid; in hypotension the cushioning effect of the fluid is lost and the cerebral mass presses on the nerve fibers, pain being caused in both instances.

In a single mechanism of irritation there can be conjointly implicated the innervation of the dura and the pia, the cerebrospinal system being represented by the trifacial, the parasympathetic by certain cranial nerves and the sympathetic by the vascular plexuses from the cervical sympathetic. Thus the pathologic physiology of headaches is brought in line with that of the visceral algias and with causalgia.

The influence of heredity, of the individual nervous constitution and the terrain must also be emphasized.

PART 3.—TREATMENT.—1. *Ophthalmology:* It almost always suffices to suppress the irritative point to relieve the headache. Thus, the headaches of glaucoma are relieved by relieving intra-ocular tension; headaches from hypermetropia yield to proper glasses, etc.

2. *Rhinology:* Here, too, removal of the cause is necessary to bring relief; the blocked sinus secretions must be given vent, a narrow nostril must be widened, compressed or irritated nerve fibers of the trifacial or sympathetic must be freed, anesthetized or destroyed. If the obstacle is of a congestive nature, and intermittent, some systemic condition must be thought of — contracted kidney, torpid liver, insufficient thyroid secretion, pelvic troubles — which appropriate therapy will relieve.

In acute sinusitis, the obstruction is almost always due to edema of the mucosa at the orifices and may be relieved by cocaine-epinephrine applications and appropriate surgery after the acute stage.

In the hyperplastic inflammations, described by Wright and Sluder, the periosteum and bone become thickened and compress the nerves in the canals and orifices at the base of the skull. Immediate relief from headaches is often obtained by cocainizing the orifice and the interior of the cavity. This should be followed by free opening of the cavity, with removal of the posterior end of the middle turbinate.

Emphasis is laid on the richness of the spheno-ethmoidal recess in sympathetic nerve elements. Often anesthesia of this region relieves remote algias, otalgia, mastalgia, vertigo, occipital and cervical pain. Even in cases in which the sinuses appear healthy but in which a sphenopalatine syndrome (sneezing, obstruction and hydrorrhea) is added to the headache, careful examination often reveals contact of the middle turbinate with the septum, the relief of which, by shrinking or removal, results in cure.

Sometimes, however, endonasal examination reveals no malformation and still anesthesia or injection of the sphenopalatine ganglion region brings relief. The

authors believe that this procedure acts through the sympathetic, causing a vasoconstriction rather than by anesthesia of the trifacial fibers. Leriche has relieved rebellious headaches by sympathectomy of the internal carotid plexus, and Sicard and Hagnenau have seen immediate relief of the pain in zona ophthalmica from periarterial sympathectomy of the temporal artery.

Finally, if the cause of the headaches cannot be found, resort can be had to diathermy, infra-red rays, massage, etc. These act by increasing local circulation, diminishing stasis and not by a direct effect on the nervous elements.

3. *Neurology:* It is only after having unraveled the participation of the most diverse local and general processes — trauma, infectious disease, diatheses, intoxications, digestive troubles, cardiovascular diseases, endocrine disturbances — that the neurologist can concentrate his attention on the mechanisms that are capable of modifying the régime of the encephalic centers and their coverings.

Two endocranial sources of headaches are discussed, meningeal irritations and tumors: (1) Meningeal irritation, either from any of the various meningitides or from infectious diseases, secondary syphilis, or exogenous or endogenous intoxications is treated by: (a) drying up the source by serotherapy, anti-infectious medications or antisyphilitic treatment, thus suppressing or reducing the access of toxins; (b) diminishing the action of toxic products in the cerebrospinal fluid by spinal or ventricular puncture and by lavage; (c) lowering the endocranial tension by puncture. (2) When the presence of a cerebral tumor is recognized, if it is demonstrated that it cannot be reached by antisyphilitic treatment or roentgenotherapy, surgical intervention must be considered. Naturally, the syndrome of hypotension will not be benefited by puncture or craniectomy. (3) Another physiologic method of treatment is the intravenous injection of hypotonic or hypertonic solutions, depending on the state of the endocranial tension; the first is followed by a raising of the tension, the latter by a lowering of it. Haden treated two cases of acute meningitis by injecting concentrated solutions of dextrose into the veins. Cushing and Foley found similar effects by administering these solutions by mouth. The effects, however, are not constant and Weed and McKibben found great individual difference in their experimental animals. Nevertheless, Claude, Lamache, Cuel and Dubar recommend intravenous injections of distilled water in cases of acute hypotension consecutive to traumatism or lumbar puncture, and the trial of concentrated solutions in certain persistent headaches and in the treatment of accidents of spinal puncture due to hypertension. Naturally, this method must be used with discretion in cases of hypertension and not substituted for lumbar puncture when it is indicated, nor cause the loss of valuable time when intervention is necessary. But in subjects who are threatened with hernia after craniectomy and in cases in which the headache is favorably influenced, one should be encouraged to use a rectal injection (drop method) of 100 cc. of a 40 or 50 per cent magnesium sulphate solution. (4) As to the various medicinal substances used to modify or forestall the effects of lumbar puncture by acting on the production or resorption of the cerebrospinal fluid, one can speak with certainty only after more accurate knowledge of these two processes has been obtained.

An article of this kind contains so many details that an abstract cannot do it justice. It will repay careful study in the original.

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PELIZAEUS-MERZBACHER DISEASE. GUSTAV BODECHTEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **121**:487, 1929.

The author mentions the cases of this disease already reported and presents the clinical picture and anatomic observations in a case of his own. The patient, a young girl, was first seen at the age of 9, when she had choreiform movements, some ataxia and slowed speech, and showed evidence of marked backwardness, being unable to answer questions at school or to feed or dress herself. The history of "nervousness" extended back for four years. All reflexes except the triceps were present. Some muscles showed spasm. Each year showed an intensifica-

tion of the choreiform movements and ataxia. Five years later, athetosis was present with the chorea. For almost the last year of life (seven years after the first examination) she was confined to bed on account of increased ataxia and attacks of dizziness. Death followed a severe bronchitis with the formation of an abscess.

The history of the patient's sister is of interest in this case. Following an attack of grip she showed the same nervous symptoms as the patient: disturbances in speech, restlessness, grimacing and inability to answer questions. She was also incontinent. The reflexes were present and normal. She was in the hospital for six months, the choreic movements and psychic state showing variability at times. There was a sudden rise in temperature accompanied by numbness, a positive Kernig sign and a poor pulse. A few days later, there was discharge of pus from the nose. On the following day she died, at the age of 5. As no autopsy was performed the diagnosis remained "chorea." The history of sixty-nine other blood relatives has been investigated, but the only information of interest is that one great-aunt had meningitis. No relationship has as yet been traced with the cases reported by Merzbacher and Bostroem.

The complete anatomic and histologic observations are given with illustrations. There is marked diffuse failure of myelin sheaths with perivascular islands and streaks of myelin-holding fibers. Under higher magnification, one finds that there is actually more myelin present than appeared macroscopically. The Meynert U-fibers are in great part disturbed, and the destroyed myelin appears as flecks and small nodules on the cortex. The great association system and commissures are also involved, the pyramidal tracts being relatively free. The axis cylinders are relatively well preserved. Some fat granule cells in the adventitial spaces indicate a slow catabolism. Glia preparations show the most marked gliosis in the same situations where the myelin preparations indicate the greatest disturbance of myelin substance. The cortex is architecturally intact. In the cerebellum, outside of sclerosis there is an atrophy shown by a paling of certain lobules, particularly of the granular layer. Outside of a slight infiltration of the meninges, there is no evidence of an inflammatory process.

Both sisters showed the onset of the disease at practically the same age, 4 and 5 years. Both showed the same outstanding symptoms. No observations of the eyegrounds are recorded.

The author does not know whether to group these two cases as diffuse sclerosis or to submit them as cases of Pelizaeus-Merzbacher disease. Literally, only the two cases belonging to the original family described by Merzbacher and Spielmeyer should be so classified, as Merzbacher stresses the hereditary factor so strongly. However, even Merzbacher included the so-called "Würzburger" case in his group. Bostroem believed that the disease leads to poorness of vision and in all his cases was able to demonstrate a temporal pallor of the papilla. Merzbacher did not believe that changes of the eyegrounds are characteristic of the disease.

Clinically, all the cases reported (including that of the author) presented twitching, continuous nodding of the head, spasm of the lower extremities and absence of abdominal reflexes. But there were, nevertheless, various individual variations, indicating that the affected motor system does not always produce the same clinical symptoms, even though the anatomic similarity is proved, when the condition is diffuse. It is almost impossible to differentiate these cases from diffuse sclerosis until the anatomic conditions are ascertained post mortem. One of the most important differentiations from multiple sclerosis is the backwardness or actual weakness of mind.

Anatomically, the great similarity between the case here reported and the Pelizaeus-Merzbacher cases lies in the presence of the perivascular myelin islets, which give the preparation its sprinkled appearance. There is a difference in the fact that the U-fibers are disturbed here and not in the Pelizaeus-Merzbacher cases previously reported. However, these and other differences might be accounted for by the fact that since only three cases of proved Pelizaeus-Merzbacher disease have been examined anatomically, a definite "constant" has not yet been reached.

In contrast to diffuse sclerosis, the characteristic feature is the maintenance of perivascular islands of myelin and certain streak-like areas of myelin sheaths.

Spielmeyer believed that in Pelizaeus-Merzbacher disease there is a slow degenerative process of the myelin substance. The process is almost exactly symmetrical. The process is a little more severe in the temporal and occipital lobes than in the frontal, and more marked in the upper than the lower half of the occipital lobe. All these peculiarities speak for an unsystematic degeneration, that is, for a process which leads to an unselective destruction of myelin sheaths. The changes in the cortical nerve cells and the meningeal infiltration are part of a secondary reaction, the author believes.

As to pathogenesis, the author does not think that he can offer a definite causative factor. That it was not infectious in his two cases he feels certain — it appeared too long after the only suggestive history, that of measles, to have been a result of this disease.

In conclusion, he believes that because of the similarities to and dissimilarities from Pelizaeus-Merzbacher disease, these cases might be offered for a group lying somewhat between Pelizaeus-Merzbacher disease and diffuse sclerosis.

ALPERS, Philadelphia.

HOW MEASURE THE SENSIBILITY OF THE SEMICIRCULAR CANAL APPARATUS? M. E. BUYS, Rev. d'oto-neuro-opht. **7**:25 (April) 1929.

The sensibility of the canals is measured by stimulating them by turning, hot or cold irrigation of the ears and galvanism, and noting the eye reflex called nystagmus. The first two methods are used most often because of the unreliability of the last; it will cause reactions in a dead labyrinth.

In rotation, the excitant is angular acceleration acting on the ampullar papillae by the inertia of the endolymph; i. e., a lagging behind of the endolymph when the turning is started and a continuation of the turning movement of the endolymph when the rotation is stopped. Thus there is a relative current between the canal and endolymph only on starting and stopping the rotation.

In the thermic or caloric method of stimulation the hot or cold irrigation warms or chills the endolymph and there is set up a current in it just as in the operation of a water heater.

Angular acceleration acts directly and almost instantaneously, the time of latency (0.006 second) representing the true latency of the reflex. In the case of thermic irrigation, the time of latency is much greater and varies with the individual conditions. It lacks precision for a quantitative analysis. In principle, rotation is more accurate; in practice, the problem is not so simple. The usual practice is to turn the patient ten turns, then stop the turning and note the post-rotatory nystagmus. One knows that nystagmus is produced by the stimulus of starting the turning (positive acceleration) and by the stimulus of stopping (negative acceleration) and that the direction of the two phases of nystagmus are opposite to each other. Being in opposite directions they tend to cancel each other. Since it is the post-rotatory nystagmus one observes clinically, in any given case this nystagmus is modified by the preceding perrotatory nystagmus and the relation between the two varies with the individual. Thus in three persons with a perrotatory nystagmus of thirty-five seconds (measured by Buys' nystagmograph) the post-rotatory nystagmus was thirty, thirty-five and eighty seconds, respectively. Therefore, one cannot use a post-rotatory nystagmus from ten turns or less to measure the sensitiveness of the apparatus of the semicircular canal. It is not practicable to continue the turning long enough to get beyond the influence of the perrotatory nystagmus. Studies with the nystagmograph have shown that, during the turning, there is, following the direct perrotatory nystagmus, a nystagmus in the opposite direction which is more feeble and of longer duration than the direct. Furthermore, in some cases this latter "inverse" nystagmus is followed by another nystagmus with the same direction as the original perrotatory and, still more exceptionally, this is again followed by another "inverse" nystagmus. One could

use the perrotatory nystagmus but it can be observed only with the aid of the nystagmograph, which is a long delicate clinical procedure. The ideal would be the production of a primary post-rotatory nystagmus equivalent to the ordinary perrotatory nystagmus, and this can be done by knowing the threshold of the acceleration stimulus and rotating the subject with an acceleration below this threshold. There will then be no nystagmus during the rotation thus practiced and when the rotation is stopped, by means of a negative acceleration, greater this time than the threshold of nystagmus, one will obtain a primary post-rotatory nystagmus.

Mulder has found the threshold for the sensation of rotation to be 2 degrees second-second. Buys has registered by the nystagmograph a feeble nystagmus with an acceleration of a little less than 1 degree second-second. He has had constructed a turning chair with which he can obtain positive uniform angular accelerations which can be varied from ½ to 2 degrees second-second, or more if necessary, and capable of a constant angular speed of thirty turns per minute. This constant speed is regulatable. The uniformly accelerated motion can be changed into a uniform constant speed at any moment of the acceleration and such constant speed maintained as long as desired. Arrest of the turning can be made in two ways: by gradually diminishing the speed in the same ratio as its increase or any other ratio, or by the use of a regulatable brake capable of stopping the turning in one-fourth, one-half or one turn. The latter procedure produces a strong stimulation of a constant value, and the sensibility of the canals would be appreciated by the nystagmus produced. The former, that of small variable excitations, seeks the most feeble excitation capable of producing a nystagmic reaction. This method stimulates both the left and the right canal system. The thermic test, in spite of its imperfections, must be used to test the canals of one side only.

A technical description of the turning chair follows.

DENNIS, Colorado Springs, Colo.

THE ANATOMY AND SYMPTOMATOLOGY OF THE EPIDERMOID CYSTS OF THE BRAIN. T. v. LEHOCZKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **122**:756, 1929.

The term epidermoid was first used by Heschl, who applied it to subcutaneous atheromas. It was later used by Bostroem to designate the cerebral cholesteatomas. Bostroem also separated the epidermoid from the dermoid tumors. Numerous ideas have been proposed to explain the origin of the cholesteatomas. Virchow and others thought that they were due to a metaplasia of connective tissue cells; Beneke and Glaser attributed to them an endothelial origin; Birsch-Hirschfeld said that they sprang from the perithelial cells of the vessels, and Chiari and Benda derived them from the ependymal cells. The most likely theories are those which derive these tumors from epithelial or endothelial tissue.

Lehoczky reports a tumor situated in the vicinity of the tuber cinereum and the interpeduncular fossa, completely filling the third ventricle and compressing the structures around the ventricle, especially the thalami, and separated from them by a fine membrane. This membrane surrounded a gelatinous mass. Microscopically, the chief part of the tumor was composed of the homogeneous, gelatinous mass, which stained a pale pink with eosin, pale yellow with van Gieson's stain and pale blue with toluidin and gave no metachromatic tint with mucicarmine. Cholesterol crystals and lacunae were not seen. Foamy cells with vacuolated cytoplasm were found in the center of the tumor, but more numerously near the capsule. In some areas they formed broad bands and a sort of transition zone between the capsule and the tumor. Plasma cells and lymphocytes were often found among them.

The membrane surrounding the gelatinous substance consisted of a fibrillary connective tissue which formed a thin, cell-poor and, in some places, hyalinized layer around the tumor. The upper part of the capsule lay close to the tela of the third ventricle, but it was easily separated from it. Below, it was adherent

to the pia. Among the fibers of the capsule were numerous infiltrative elements—plasma cells and lymphocytes. In the greater part of its extent the capsule was lined by a single layer of cells. In places these cells were small and linear and in others large and polygonal, with clear, oval nuclei. In many places the cell layer was multiple; Lehoczky believes that these cells are epithelial. Small epidermal islands were found here and there around the capsule, and a strip of epidermis with two layers of the skin: the stratum germinativum and the stratum granulosum.

Lehoczky states that the gelatinous mass that comprises the main portion of the tumor is a product of the epithelial cells of the capsule, and is produced by a dissolution and degeneration of these cells. The origin of the epithelial cells and epidermal islands in the capsule is not easy to determine. Two possibilities present themselves: (1) they arise from the epithelial infundibular islands of Erdheim, or (2) they represent embryonic germ cells. They are not derived from the cells of the infundibulum, which Erdheim has demonstrated to be normal rests in the development of the hypophysis. The epithelial islands are probably due to aberrant epithelial cells formed in the closure of the neural tube. The situation of the tumor in the midline and the histologic nature of the neoplasm indicate this clearly.

Lehoczky asks what criteria differentiate the cholesteatomas from the epidermoids. The presence of cholesterol does not seem to be important; Virchow believed so at any rate, but Bostroem claimed that there was no cholesteatoma without cholesterol. Lehoczky defines a cholesteatoma as a tumor with a pearly surface, with mother-of-pearl-like, glancing, dry, crumbly contents, arranged like an onion or concentrically; they contain cholesterol and possess a fibrous capsule lined with epithelium. While the conception of the cholesteatoma seems well defined, that of the epidermoids is vague. Some investigators, following Bostroem, look on epidermoids as cholesteatomas, others as dermoids. Hofmeister used the term epidermoid to mean certain tumors that are closely related to the cholesteatomas but differ from them. Lehoczky suggests that the term epidermoid should be used to designate a tumor independent of the cholesteatomas. "The cerebral epidermoids form an independent group which possesses exact characteristics like the cholesteatomas, and are to be differentiated from other groups." He points out further that the contents of the cholesteatomas are due to cell activity and that of the epidermoids to degeneration. It is striking that in the epidermoid tumors there is so little evidence of cornification.

ALPERS, Philadelphia.

SYMPTOMATIC PARKINSONISM. E. BRZEZICKI, Schweiz. Arch. f. Neurol. u. Psychiat. **25**:36, 1929.

In this article, the fourth of a series on the same subject, the author discusses parkinsonism associated with tumors of the brain. In an introductory statement he says that, in general, it is almost impossible to draw positive conclusions in regard to localization from the symptoms of tumor, especially if the growth is large and signs of pressure exist in addition to those of focal origin. While tumors of the basal ganglia can no doubt produce extrapyramidal symptoms, cases of such tumors without the corresponding symptoms have been published. Hyperkinesias in tumors of the basal ganglia are rare, the location being either in the brachium conjunctivum or the red nucleus in the cases so far reported. On the other hand, akinesias are more common, especially in tumors of the striopallidum, thalamus and substantia nigra. Most authors seem to believe that the akinesia described in cases of tumor of the frontal lobe is due to pressure on the neighboring basal ganglia.

In case 1 was presented a slight left hemiparesis and parkinsonian symptoms confined to the upper part of the body. There was a slight tremor of the right arm which was more rigid than the left. At autopsy, a spongioblastoma multiforme was found which apparently had arisen in the right frontal lobe, invaded the left and destroyed the head of the caudatum and pallidum on the left side. The limitation of the parkinsonism to the upper part of the body thus corresponded

to the Vogt theory of localization in the basal ganglia. The frontopontile tracts were intact.

In case 2 was presented a right hemiplegia with severe pain in that side of the body in addition to a generalized parkinsonism, but no tremor. At autopsy a sarcomatous tumor, destroying the greater part of the right thalamus, globus pallidus and putamen, was found. There was also unilateral degeneration of the substantia nigra, which the author believed was retrograde, as no direct pressure had been exerted by the tumor on this region of the brain.

In case 3, a girl, aged 20, gave a history of measles encephalitis at the age of 5, with a right hemiplegia as a residuum. Headache commenced at the age of 10, and when the patient was 17 she developed a hemiparkinsonism on the right side. On admission, the tremor and other parkinsonian features were unmistakable in spite of the hemiplegia. At autopsy, the left frontal lobe was found to be almost entirely replaced by a huge cyst which had destroyed the striopallidum in its anterior and middle portions. This cyst, which was lined with ependyma, seemed to be due to an inflammatory closure of the foramen of Monro.

Case 4 was similar to the foregoing case in that there was a history of encephalitis followed by left hemiplegia. The patient presented a parkinsonian syndrome with tremor, the plastic tonus being especially marked on the left side. Autopsy revealed a multilocular cyst of the right frontal lobe extending into the insula and bringing about pressure atrophy of the basal ganglia.

The author states that he has seen two other patients in whom there was no parkinsonism, although the striopallidum of one side had been almost completely destroyed by glioma. Since a lesion of but one of the basal nuclei in some cases seemed to bring about a unilateral or bilateral parkinsonism while grosser lesions in other cases failed to do so, the author suggests that in the former case an important, but at present unknown "Schaltungstelle" for many centers may have been destroyed. When the process was more extensive other centers may have been activated to perform the functions of the destroyed parts.

DANIELS, Rochester, Minn.

SLEEP AS A PROBLEM OF LOCALIZATION. C. VON ECONOMO, J. Nerv. & Ment. Dis. **71**:249 (March) 1930.

Using the word "centre" as an accumulation of nervous gray matter of importance in the production of some definite function, the author considers the evidence adequate for such a regulatory center for the biologic condition of waking and sleeping in the region of the third ventricle. There have been many theories concerning sleep. Exner and Robl Rükhard considered that the ganglionic cells of the brain retracted their dendrites like pseudopodia. Purkinje believed that arterial congestion produced by substances in the blood and located in the thalamus and corpus striatum exerted pressure on the fibers of the corona radiata, thus strangulating and interrupting the conduction of impulses to and from the cortex. Mauthner assumed that the interruption in conduction took place in the region of the aqueduct in the midbrain. Besides the theory of lack of stimuli, there are the chemical theories of Pflüger and DuBois Reymond in which asphyxiation of the brain with carbon dioxide was postulated. The last of these theories was advanced by Piéron, who extracted from exhausted dogs a substance that produced sleep when injected into healthy dogs and which he called "hypnotoxine." Since that time, the narcotic action of carbon dioxide and lactic acid has become known.

The following facts remain unexplained by the theories cited. Sleep can be produced in naps without fatigue. Sleep is reversible and hence does not represent a mere narcotic action in which this reversibility does not exist. Syncope, coma, cerebral concussion, etc. do not show the reversibility characteristic of normal sleep. Mingazzini and Barbara assumed that the periodicity of sleep was produced less by a fatigue substance than by endocrine processes acting on the vegetative system. Other periodic functions of the body, such as ovulation, mating and menstruation, which are independent of the central nervous system, are familiar.

In 85 per cent of cases of epidemic encephalitis, there is some trouble of the sleep function; sopor of all degrees has been observed extending for weeks and even months. In these cases inflammatory lesions have been found in the cup of the midbrain at its juncture with the thalamus. Combinations of chorea and insomnia were found associated with lesions of the lateral wall of the third ventricle near the corpus striatum. Inversion of sleep periodicity was a frequent symptom. The author considers it wrong to attribute this somnolence to the toxic effect of the disease, because Wernicke's disease, Gayet's disease and tumors of the infundibulum frequently present sopor. Hence, he concludes that it is not the individuality of encephalitis itself so much as the localization at this definite area of the nervous system that is responsible for the sleep.

In all probability, the "centre" coordinates the changes occurring in sleep. Pavlov's observation that repeated interruption of conditioned reflexes produces an inhibitory action on the cerebral cortex and later sleep brings the author to assume that the function of this center is inhibition of the cortex and thalamus, and that the function is started ordinarily and normally by a fatigue substance circulating in the blood, the periodicity of which is "anchored" in the vegetative system. He places this center in the most frontal part of the nucleus oculomotorius, extending frontad to the gray walls of the third ventricle into the hypothalamus. Recent experiments of Hess, in which cats have been made to yawn and assume positions of rest on electric stimulation by weak currents of the anterior region of the aqueduct and the posterior wall of the third ventricle, tend to confirm the author in this localization.

HART, Greenwich, Conn.

A METHOD OF RECORDING MOTOR EXPRESSIONS IN NEUROLOGIC EXAMINATIONS. M. S. LEBEDINSKY and A. R. LURIA, Arch. f. Psychiat. **87**:471, 1929.

The authors have devised a method for the purpose of recording the motor concomitants of verbal responses in association experiments. The Jung word-association test is used. The patient is placed in a comfortable position with a pneumatic bulb grasped in the right hand. This is connected to a lever which records variations in pressure on a revolving kymograph. The patient is given the stimulus word and is told to respond with the first word that comes into his mind and at the same time as he reacts with the word he is to press the bulb. The results of the investigations were:

1. In normal persons there is usually a variation between a smooth line preceding the up-stroke (produced by the pressure accompanying the verbal response) and a slight unsteadiness in this line.

2. The first and most interesting pathologic results were found in cases of hysteria. It is, of course, well known that the reaction time of hysterical patients in the Jung association test is characterized by extreme variation, being very short at times and at others extremely long. In the authors' experiments they were able to show that during this reaction-time period there are repeated up-strokes from the base line which sometimes develop into an irregular wavelike progression toward the final up-stroke when the word is given. This suggests the possibility that a number of other words come to the surface but are repressed until the final response is given. At times even the final pressure on the bulb is repressed and the up-stroke appears after the verbal response is given.

3. Neurasthenia: Under this heading the authors group all psychoneurotic reactions that do not belong to the classic hysterical picture. Here one finds a more stable reaction-time period, although it is not quite as stable as in normal persons. During this period there is usually a finer, more diffused spread of a wavelike motion which finally culminates in the up-stroke corresponding to the verbal response.

4. Organic diseases: In patients with motor aphasia three variations in the test were carried out. In the first the patient was told to repeat the word given and press on the bulb at the same time. This produced a tracing which was fairly

near the normal, although there were certain breaks in the line. Still nearer to the normal picture were the results when the patient was told to press on the bulb in response to the stimulus word without attempting to answer. When the patient was told to respond with some association to the stimulus word the reaction-time period became very long and the tracing during this reaction-time period as well as the final response resulted in a quivering, irregular conglomeration of up and down strokes. A more or less similar series of results were obtained in a case of stuttering. In dementia paralytica an increased reaction-time period, with a slowly mounting up-stroke sometimes broken by tremor, was observed. In postencephalitic and parkinsonian patients an irregular reaction-time period and a tendency to repeat the up-stroke between the stimulus words were noticed. No particularly significant observations were obtained from the epileptic patients outside of a diffuse tremor that was not unlike the neurasthenic patients.

MALAMUD, Iowa City.

ACUTE BILATERAL RETROBULBAR NEURITIS IN A HYSTERIC (ETIOLOGIC CONSIDERATIONS). BASILE DIMISSIANOS, Rev. d'oto-neuro-opht. **7**:440 (June) 1929.

In the following case, it is impossible to say whether there was an acute organic or a purely functional retrobulbar neuritis. A woman, aged 21, whose family history was unessential, gained 53 pounds (24 Kg.) in one year at the age of 15 and has retained this weight. The menses had always been abundant, irregular and painful. On June 28, 1926, movement of the left eye was painful, the pain being located in the upper palpebral furrow. Ten days later, dimness of vision appeared and the eye was completely blind within six days more. Eight days after the blindness appeared, the pains ceased. On August 6, an examination of the eye revealed normal vision in the right eye, perception of motion in the left eye and normal eyegrounds and the reaction to light in the left pupil was less than in the right. On August 30, pain appeared in the right eye but the vision remained normal. The Wassermann reaction of the blood and spinal fluid was negative. Neurologic, rhinologic and otologic examinations gave negative results. A roentgenogram showed a homogeneous shadow in front of the petrous bone. During antisyphilitic treatment, peripheral vision in the left eye returned and by October 8 the vision was 6/10. In the meantime, vision in the right eye was reduced to perception of the fingers at 1 m. with a central scotoma. By November 19, the central scotomas had disappeared and vision in each eye was 5/10.

The patient entered the clinic in November, 1928, because of pain from muscular asthenopia. The pain had begun a few days before, was present in both palpebral furrows and was increased by lateral movements of the eyes. An examination of the eyes showed 5/75 vision in each eye, corrected to 5/5 by glasses. The only other abnormality was a defect of accommodation of 6.5 diopters in each eye separately and of 7.5 diopters for binocular vision. The two papillae were perfectly normal. The basal metabolic rate was slightly diminished (— 19 per cent). Medical, neurologic and roentgenologic examinations gave negative results. It was ascertained that sixteen months before the first appearance of the retrobulbar neuritis, the patient had been treated for hysterical aphonia.

In cases of atypical retrobulbar neuritis one should think of a disease of the cranial base, but this could be ruled out; the sella was normal and there was no local sign of disease of the hypophysis; the sinuses were normal and there was no evidence of organic lesion, endogenous or exogenous toxemia or of lesion of the nervous system. Syphilis was ruled out by the negative Wassermann reaction and the therapeutic test. There remained only the supposition of hysteria, supported by the previous history of hysterical aphonia and the presence of muscular asthenopia. On the other hand, it is rare to see patients with retrobulbar neuritis recover, and the condition leave no diminution of vision, dyschromatopsia or changes in the nerve head. Again, this disease lasts at the most six weeks, while vision in the case in question recovered only after six months. In spite of all this, the

author hesitated to accept the diagnosis of hysterical retrobulbar neuritis. The majority of writers deny the functional origin of this malady. It is possible that sooner or later organic lesions will appear. DENNIS, Colorado Springs, Colo.

BIOLOGIC STUDIES OF THE BLOOD IN THE AFFECTIVE PSYCHOSES. D. BOGEN, Rev. Psychiat., Neurol. & Reflexol. (Leningrad) **4**:78, 1929.

In the series of experiments undertaken by the author, twenty-three patients were studied; eleven patients were very depressed, three were in a manic state, one was in a mixed state, one in a mild hypomanic state, and seven were in a mild depressed state. There were fourteen women and nine men. The aim of the examiners was to determine the relative content of epinephrine as well as of sugars in the blood. The work was inspired by a recent translation of Cannon's book into the Russian. A small piece of the intestine of a cat was put in a beaker containing Ringer-Locke's solution. The intestinal strip was connected with a recording device which transmitted the contractions to a kymograph. Standard curves were obtained and used for comparison. The blood was taken from the patients while fasting and immediately defibrinated. In the preliminary control experiments it was found that there was an inhibition of the intestinal peristalsis when the concentration of epinephrine was 1 to 400,000,000. In concentrations of 1 to 10,000,000 complete cessation of contractions took place.

In three depressed patients and one manic patient, definite inhibition of the peristaltic waves took place, such as one finds on the addition of epinephrine to saline solution in concentrations of 1 to 30,000,000. In nine patients the curves deviated markedly from the normal, and in two patients perfectly normal curves were obtained.

In eighteen patients the blood sugar in fasting was determined by the Hagedorn-Jensen method. The normal variation in this determination is from 80 to 110 mg. per hundred cubic centimeters of blood. In thirteen patients the blood sugar was above the limits of normal.

The experiments dealing with the epinephrine content of the blood were repeated from time to time on the same patients; the curves varied with every experiment. The author expressed the belief that the vegetative nervous system in his patients was in a continual state of flux. He is not able to explain the significance of the abnormal curves obtained from some patients and believes that other mechanisms may be at work. The presence of definitely increased amounts of epinephrine in four cases indicates that epinephrine may be stable; with finer methods of determination there may be more evidence of the presence of increased amounts of epinephrine in the affective psychoses. KASANIN, Boston.

SOME FUNCTIONAL PROBLEMS ATTACHING TO CONVERGENCE. CHARLES SHERRINGTON, Proc. Roy. Soc. **105s.B**:332 (Sept.) 1929.

In the first Ferrier lecture Sherrington reports his researches on some functional problems attaching to convergence. He considers convergence and motor neurons; occlusion of contraction; occlusion as an index to reflex overlap; summation of subliminal excitation; time relations of the "central excitatory state"; confluence of excitatory with inhibitory path, and several other phases. One section is devoted to "Inhibition Selectively Arrests Those Activated Motor-Units which are Under Weaker Central Excitation."

He describes experiments from which the following conclusions are drawn: "Though trains of impulses are the sole reactions which enter and leave the central nervous system, nervous impulses are not the sole reactions functioning within that system. States of excitement which can sum together, and states of inhibition which can sum together, and states which represent the algebraical summation of these two, are among the central reactions. The motoneurone lies at a focus of interplay of these reactions and its motor unit gives their net upshot, always expressed in terms of motor impulses and contraction. The

central reactions can be much longer lasting than the nerve impulse of nerve-trunks. Further, these central states and reactions are, as compared with the processes of nerve-trunk conductions, relatively very sensitive to physiological conditions, and are delicately responsive to fatigue, blood supply, drugs, etc. The specific cell units, the neurones, far from behaving merely as passive recipients and transmitters of impulses, modify as well as transmit what they receive. They can develop rhythm of their own, and their rate of discharge can rise and fall with intensity of central excitation and inhibition respectively."

BERENS, New York.

CALCIUM STUDIES. A. CANTAROW, Arch. Int. Med. **44**:667 (Nov.) 1929.

A study of sixty-eight normal persons demonstrates that the calcium content of the cerebrospinal fluid is rather constant, averaging 5 mg. per hundred cubic centimeters, and seldom varying by more than 0.5 mg. Even in disease there is little variation, and what there is is almost entirely in the direction of increase. Thus, thirty-five patients with cerebrospinal syphilis, tabes or dementia paralytica showed an increased calcium content in all but seven; of eleven in the meningitis-encephalitis group, ten had a high concentration of calcium. The author then proceeds to study the relationship between blood and spinal fluid calcium, showing that the normal relationship is 10:5, i. e., the ratio is 50 per cent. Working on the theory that the spinal fluid is a filtrate of the blood and not a secretion, Cantarow shows that there is a slight but definite increase in this blood-spinal fluid ratio in many nervous and mental diseases. From this the conclusion would be that there is an increased permeability of the choroid plexus. The ratio varies from 55 in some cases of tabes to a ratio of 68 per cent in a case of alcoholic psychosis. In the light of Malamud's recently reported work on the permeability quotient in epilepsy, it is interesting to see that Cantarow found an increased diffusibility in only one of his four epileptic patients. In a report published in the same journal the following month (**44**:834, 1929), he takes up the problem of parathyroid extract and its influence on this diffusibility. After working on eleven patients, Cantarow finally concluded that parathyroid gland extract will cause temporary increase in the blood-spinal fluid calcium ratio, but that this will be followed by a prolonged decrease in this ratio. These experiments also affirm the previous conclusions that introduction of parathyroid causes an increase in the amount of blood calcium.

DAVIDSON, Philadelphia.

CEREBRAL HEMORRHAGE FROM VENOUS AND CAPILLARY STASIS. STANLEY COBB and JOHN P. HUBBARD, Am. J. M. Sc. **178**:693 (Nov.) 1929.

Five cases of hemorrhage into the brain substance from congested veins and capillaries are presented. Case 1 was that of a woman, aged 46, who after bronchopneumonia developed an extensive phlebitis of the legs, abdomen and finally in the veins of the dura and brain. Two large areas of softening associated with sinus thrombosis were found. Owing to the venous stasis there was a damming back of blood into the smaller vessels and a consequent hemorrhagic extravasation and softening. Case 2 was that of a girl, aged 2¼ years, who developed meningitis after a case of otitis media. Microscopic examination of the brain showed a purulent exudate over the surface, thrombosis of the cortical vessels and circumscribed hemorrhage. Here the thrombosis was the result of meningeal infection. Case 3 was that of a girl, aged 14 months; vomiting was followed by unilateral convulsions two days later. Extensive arachnoid hemorrhage with congested and thrombosed surface vessels, doubtless due to venous stasis, was present. Case 4 was that of a woman, aged 86, who was asphyxiated with illuminating gas. The conditions were similar to those usual in carbon monoxide poisoning but with unusual extensive areas of hemorrhage and softening in the cortex. Case 5 was that of a male infant, aged 1 day, who had convulsions after prolonged asphyxia.

Intense congestion was found of all blood vessels throughout the brain, with more in the veins than in the arteries.

These five cases show the necessity of bearing in mind that subarachnoid hemorrhage may have its origin in the venous system. The two main factors concerned are venous stasis and asphyxia; the unit lesion is a petechial extravasation and large lesions are formed by coalescences.

MICHAELS, Detroit.

PSYCHOGENICALLY CONDITIONED SPONTANEOUS HEMORRHAGES OF THE SKIN. E. JACOBY, Arch. f. Psychiat. **88**:631, 1929.

The author reports two cases of spontaneous cutaneous hemorrhages. The first case was that of an unmarried woman, aged 34, of a sensitive make-up and a poor adjustment. For the last few years preceding admission to the hospital she had had a number of economic difficulties. On several occasions, when these difficulties reached acute crises, the patient would show marked emotional disturbances. Afterward, there would be fairly large areas of subcutaneous hemorrhages, which were definitely associated with the emotional disturbances. They would begin after such an upset and the patient would first be conscious of a pain in the region where the hemorrhage would subsequently show itself. In the hospital, under general care and away from difficulties, these did not occur. Once, however, it was possible to elicit hemorrhages under an experimentally arranged situation. When she was discharged from the hospital and went out to meet her previous difficulties, the hemorrhages reappeared. Case 2 was that of an unmarried woman, aged 25. Since the age of 11, she had shown compulsion phenomena of various types which became more serious as time went on; before admission, symptoms of a psychotic nature began to develop. In this case, too, subcutaneous hemorrhages were reported and discovered on examination.

The author is of the opinion that these hemorrhages are psychogenic in origin and represent substitute reactions in these patients. They should be regarded in the same light as other hysterical manifestations. Just why a patient should choose this form of reaction in preference to the other more usual hysterical manifestations remains a question that the author does not attempt to answer.

MALAMUD, Iowa City.

COLORED AUDITION IN ART AND PSYCHIATRY. J. S. GALANT, Fortschr. d. Med. **47**:965 (Nov. 29) 1929.

Colored audition is a phenomenon, according to the author, that rests on the boundary between the normal and the pathologic. Gahlbeck believes it to be a capacity of great importance for artists and musicians in producing an inner harmony between the stage and music. This writer analyzes the music of Beethoven, Wagner, Strauss and Brahms in terms of color. Each musical instrument is supposed to evoke a specific color feeling in the listener. Thus, the trumpet produces red, the oboe a sharp chrome yellow, the flute a blue and the cello brown. An orchestration thus becomes a complex picture. Some psychiatrists have regarded the phenomenon as pathologic and hallucinatory. Korsakow regarded it as a qualitative perception disturbance and considered it analogous to the irradiation of sensory impulses that one may get, for instance, in a toothache which becomes referred to various branches of the trigeminal nerve. These secondary feelings or synesthesias, according to him, are normal phenomena. He describes the case of the Nussbaumer brothers who experienced with each auditory perception a corresponding color perception. Certain tones to them were less pleasant than the color perceptions accompanying them. Other persons with similar colored audition proved to be psychopathic personalities, with abnormally stimulated fantasy production. Colored audition is not regarded as abnormal by the author as it is seldom observed in psychotic cases, but as a peculiarity of the

human psyche which gives the impression of abnormality. Bleuler also considers that the phenomenon has nothing to do with hallucinations and has no pathologic significance.

HART, Greenwich, Conn.

MALARIAL THERAPY IN SCHIZOPHRENIA. A. WIZEL and R. MARKUSZEWICZ, Jahrb. f. Psychiat. u. Neurol. **46**:255, 1929.

This paper is the authors' report of their second series of experiments on the treatment of schizophrenia with malaria. The material consisted of forty patients with acute, and seventeen with periodic schizophrenia; in addition to this, fifteen patients with chronic schizophrenia were inoculated in order to preserve the malarial organism. The authors designate as acute those cases the duration of which was not longer than one year, and as periodic those characterized by one or more exacerbations.

Nine of the forty patients with acute cases showed a good remission, eleven an incomplete and eight a slight remission, and twelve showed no improvement. Nine of the seventeen patients with periodic cases presented a good remission, three a slight remission, and five were unaffected. Of the fifteen patients with chronic cases who had been inoculated for other than therapeutic reasons, two showed a slight remission and two an incomplete one. In the entire series, then, remissions occurred in 50 per cent of the acute, and in 70.6 per cent of the periodic, cases.

The authors find that the greatest number and the longest remissions are obtained in cases in which malarial therapy is resorted to early, if possible before the patients have been ill for six months. They also find that the best and longest remissions are obtained when the patients are allowed to have as many as twenty attacks of chills and fever. This applies to those with acute, as well as those with periodic, schizophrenia.

KESCHNER, New York.

PSYCHOTHERAPY IN THE TREATMENT OF CHRONIC ALCOHOLISM. R. R. PEABODY, Ment. Hyg. **14**:109 (Jan.) 1930.

The difference between the "hard drinker" and the person with chronic alcoholism is, in the author's opinion, more than a merely quantitative one. The hard drinker may take liquor every evening, but it is largely a social rite. The chronic drinker, on the other hand, likes to drink in the morning; sleep, which is the end of a spree to the hard drinker, is but the interval between drinks to the chronic drinker. Being deprived of alcohol is an annoyance to the hard drinker; the other drinker faces that prospect with deep dread. When the drinker realizes that liquor is medicine for mental suffering, he has taken the first step toward chronic alcoholism. Such persons usually have some inferiority to begin with, and seek self-aggrandizement and fulfilment of a wish by the easy method of intoxication. In their search for irresponsibility they present a childishness which characterizes alcoholism both in the acute and in the chronic phases. Most chronic drinkers are introverted, and drink to extrovert themselves; the others drink to extrovert themselves still further. In the causes of alcoholism, Peabody believes that heredity is of minor importance, and the influence of an early alcoholic environment is only of little more significance. The patient has an unpleasant emotional conflict; like the neurotic person he tries to escape it, but he lacks the courage. The treatment consists in an analysis of the precipitating factors, in physical relaxation, in suggestion, in persuasion and in the development of outside interests by the promotion of reading, hobbies and exercise. Peabody believes that given an intelligent and integrated patient, the outlook should be hopeful.

DAVIDSON, Philadelphia.

THE BLINKING REFLEX IN HEMIPLEGICS. HOLGER EHLERS, Acta psychiat. et neurol. **4**:47, 1929.

Ehlers classifies closing movements of the eyelids into two types: winking, which is a slow, even closing due to the action of the palpebral portion of the orbicularis muscle and is usually voluntary; blinking, a rapid movement, usually reflex, and squeezing, due to the acting—usually voluntary—of the whole orbicularis muscle. The motor pathway for reflex blinking movements is the facial nerve; the sensory, either from contact, stimulation transmitted through the trigeminal nerve, or by a strong light stimulus or threatening visual impressions through the optic nerve. The pathways connecting the optic and trigeminal nerves with the facial nerves are unknown. He found in patients with hemiplegias that the blinking reflex is altered without hemianopia or disturbances of corneal sensibility. In some patients, the reflexes elicited by both contact and light stimuli were diminished; in others, one was reduced and the other average, and in still others those elicited by strong light were increased. Therefore, in those hemiplegic patients, the disturbance of the blinking reflex lay in the sensory rather than the motor portion of the arc. There is no precise explanation for these observations. They seem to indicate that there may be long pathways extending into the hemispheres for these reflexes. The author points out that examination of the blinking reflex is used for determining the presence of hemianopia. His observations indicate the dubious value of the test in patients with hemispheric lesions, because the reflex may be reduced or increased even if no hemianopia is present.

PEARSON, Philadelphia.

NASAL SPRAY METHOD OF ADMINISTERING HORMONES OF THE OVARY AND PITUITARY GLAND. J. P. PRATT and M. SMELTZER, Endocrinology **13**:320 (July-Aug.) 1929.

The use of ovarian and pituitary hormones over an extended period of time might be secured, it was considered, by absorption from the mucous membranes. Since the absorption is relatively slow, the action of the hormone would be more prolonged than when given either hypodermically or intramuscularly. The authors consider that the nasal spray method is better than nasal pledgets, since the pledgets cause a local reaction and production of mucus which checks the absorption. Several cases are presented to indicate that the treatment is as satisfactory if not more so than by hypodermic injection; the patients were more enthusiastic about it than about other types of treatment. These cases also illustrate its efficacy. The hormones used were proprietary ovarian and pituitary hormones. The ovarian hormone was used in cases of amenorrhea and menstrual disturbances of this type. The pituitary hormone was used for the control of diabetes insipidus and for the control of uterine hemorrhage, particularly menorrhagia and metrorrhagia. In a few patients it was considered that the mucous membrane of the vagina was preferable, but the reason given for this choice was psychologic. They concluded that this administration was so simple that the patients would have no difficulty in managing it at home and that the field of activity of these hormones was greatly increased by the ease of administration.

WAGGONER, Ann Arbor, Mich.

CONVULSIVE STATES: A CLINICAL STUDY OF UNUSUAL PHENOMENA, ETIOLOGY, DIFFERENTIAL DIAGNOSIS, AND TREATMENT. A. E. BENNETT, Am. J. M. Sc. **178**:677 (Nov.) 1929.

In 200 cases of the convulsive state, 124 were classified as essential epilepsy, 11 as hysterical, 9 as traumatic and 56 as definitely organic. Twenty per cent of the cases presented definite physical factors, such as focal infection, promoting epileptic seizures; only 15 per cent of the patients gave a history of infantile spasms. Of the 124 essential epileptics, 18 per cent showed distinct mental reactions aside from the usual epileptic personality; a definite history of migraine was obtained

in 10 per cent of the cases. A group, 7.2 per cent, with convulsions due to cardiovascular disease, either arteriosclerosis or hypertension, seemed high, while only 3.5 per cent of the entire group was classified as having cerebrospinal syphilis. An accurate organic diagnosis was not possible in 5.5 per cent of the cases. In 6 per cent of the cases, convulsions occurred as manifestations in brain tumor or abscess.

In the management of convulsive states the main issue first is to eliminate all possible organic and toxic causes. Drug therapy is used mainly to lower the threshold of cortical irritability. Sufficient bromide, up to about 60 grains a day, or phenobarbital, up to 3 grains a day, should be given to control the seizures. Not much stress is as yet warranted in the extreme restriction of the diet. In status epilepticus drastic measures may be resorted to, such as strenuous elimination and large doses of sedatives.

MICHAELS, Detroit.

EYE MANIFESTATIONS IN FRACTURE OF THE SKULL. GEORGE A. BLAKESLEE, Arch. Ophth. **2**:566 (Nov.) 1929.

The neurologist should be consulted more often in cases of fractured skull, for a careful neurologic examination often reveals signs of great prognostic importance. Owing to the frequent unconsciousness of the patients, examination of the eyes is a peculiarly valuable procedure. Blakeslee groups his ophthalmic observations into six classes: ecchymoses, extrinsic eye-muscle palsies, nystagmus, scotoma, changes in the disk and pupillary phenomena. Ecchymoses into the lids are frequent but of little prognostic value. Oculomotor signs are suggestive of brain injury, not necessarily basal. Nystagmus was infrequent. Scotomas and changes in the disk were of minor importance, papilledema occurring less often in acute depressed fractures than might be expected. Pupillary phenomena, on the other hand, were of considerable significance. Blakeslee comments on the striking variation in the pupillary symptomatology, a variation occurring sometimes at almost hourly intervals. When the pupils were fixed and dilated, the prognosis was poor—95 per cent of his patients in this group died. A unilateral, dilated, fixed pupil was found in both epidural and subdural hemorrhage. Inequality of the pupils was a common observation, due, Blakeslee suggests, to central cortical pressure rather than to pressure on the third nerve. His final conclusion is that, as a general rule, a positive eye symptom in a patient with fractured skull suggests a poor prognosis.

DAVIDSON, Philadelphia.

VARIATIONS IN THE MUSCULAR TONUS IN VENTRICULAR HEMORRHAGES. T. DOSUŽKOV, Rev. Psychiat. Neurol. & Reflexol. (Leningrad) **4**:175, 1929.

The author reports the case of a woman, aged 61, who had had a cerebral hemorrhage with a residual hemiparesis on the right side. While under treatment in the neurologic clinic, the patient had another cerebral accident. On examination it was found that she was unconscious and spastic on both sides, with a bilateral Babinski sign. The knee reflex was absent on the right but hyperactive on the left side. Half an hour later, the patient was flaccid; there was a bilateral Babinski sign; the knee jerk was increased on the right and absent on the left side. For two and a half hours, until the patient died, this marked alteration in the tonus of the peripheral musculature was noted every fifteen or twenty minutes. Marked flaccidity alternated with spasticity. The patient also presented meningeal signs, and for this reason a diagnosis of a hemorrhage into the ventricles was made. The diagnosis was confirmed by autopsy.

The phenomenon of an alteration of spasticity and flaccidity was first described by Davidenko, in 1919, under the name of hormetonia (attacks of hypertonia). The condition is usually found in grave involvements of the cerebrum preceding death. The phenomenon is analogous to experimental decerebrate rigidity in animals. Thus far, seventeen cases have been reported in the Russian literature.

KASANIN, Boston.

DIPLEGIA FACIALIS IN EARLY SYPHILIS. M. J. STRAUSS, Arch. Dermat. & Syph. **20**:306 (Sept.) 1929.

Pointing out that bilateral seventh nerve palsy due to syphilis is extremely rare, Strauss reviews the only other cases of this condition previously reported—thirty-five of them—and adds another. In the author's case, a man, aged 43, showed a peripheral right facial palsy and within a few days developed paralysis of the left side as well. He had nocturnal headache, an irregular left pupil and bilateral spasticity. He received mercuric succinimide and a course of injections of neoarsphenamine. Within a month of the onset, the facial symptoms had entirely disappeared. Strauss considers the possibility of the facial involvement being due to the mercury or to the arsenic, but after reviewing the reasons offered for this contention he rejects it, emphasizing rather the point of view that the cranial nerve involvements in syphilis are due to invasion by the disease process.

DAVIDSON, Philadelphia.

COMBINED LARYNGEAL PALSIES: REPORT OF A CASE OF VILLARD'S SYNDROME DUE TO A NEUROMA ON THE LAST FOUR CRANIAL NERVES. REIDAR SCHROEDER, Acta psychiat. et neurol. **4**:163, 1929.

Villard, in 1917, described a syndrome consisting of paralysis of the pharynx, larynx, soft palate, tongue, sternocleidomastoid and trapezius muscles, and the sympathetic nerve, to which he gave the name of the syndrome of the nerves of the posterior retroparotid space. The author reports an instance of this syndrome associated with adiposogenital dystrophy in a man aged 25. At necropsy, a neurofibroma in the retroparotid space, which had involved the ninth, tenth, eleventh and twelfth cranial nerves, was found. He believes that the association of systemic anomalies with the neurofibroma in this case lends weight to the view that the tumor itself results from some systemic congenital deficiency.

PEARSON, Philadelphia.

LIGHT THERAPY IN MENTAL HOSPITALS. H. DOVE CORMAC, J. Ment. Sc. **75**: 410 (July) 1929.

Actinotherapy is considered a necessary adjunct to the treatment in mental cases. Results, covering four years, showed marked and general increase of body weight, improvement of appetite and increased muscular activity. Blood pressure records indicated a slight average decrease in the systolic pressure. The metabolic rate and blood counts showed no constant variations. Manic-depressive cases responded most readily, and periods of depression appeared to be curtailed; patients with irritability from delusions became more amiable; some patients with dementia praecox showed greater motor activity. Depression with agitation, and signs of hyperthyroidism were sometimes exaggerated.

SINGER, Chicago.

INTRACRANIAL HEMORRHAGE IN THE NEW-BORN INFANT AS DEMONSTRATED BY THE ROENTGEN RAYS. M. H. ROBERTS, Am. J. Dis. Child. **38**:1196 (Dec.) 1929.

By injecting metallic mercury, red lead solutions or iodine salt-oil preparations into the carotid artery of infants who have died of intracranial hemorrhage and then taking x-ray photographs, Roberts finds it possible to visualize the arterial tree and to localize the site of the hemorrhage and estimate its extent. This procedure is available in cases in which an autopsy permit is not obtained. The article is accompanied by six illustrative x-ray photographs.

DAVIDSON, Philadelphia.

THE TREATMENT OF CHOREA WITH PHENOBARBITAL AND MAGNESIUM SULPHATE: CONSIDERATIONS ON THE PHYSIOPATHOLOGY OF CHOREA. G. MARINESCO, O. SAGER and G. T. DINISCHIOTU, Ann. de méd. **27**:237 (March) 1930.

The authors report five cases of Sydenham's chorea which reacted favorably to subarachnoidal injections of magnesium sulphate within from five to six day intervals (0.008 mg. per kilogram of body weight in 25 per cent solution). Another therapeutic attempt was the subcutaneous injection of phenobarbital, 0.22 cg. of sodium phenobarbital dissolved in 1 cc. of distilled water. The injections were repeated every other day for from twenty to twenty-five days. A discussion of the etiology of chorea is added, based on the theories of Minkowski, Foerster, Wilson and others.

WEIL, Chicago.

PSYCHIATRIC CLINIC AND JUVENILE COURT. JAMES PLANT, Ment. Hyg. **13**:708 (Oct.) 1929.

The interests of society will be served, Plant believes, not by closer cooperation between the psychiatric clinic and the juvenile court, but rather by a presentation of opposite points of view. The judge wants to know: "Did the child do this?" and the psychiatrist wants to know "Why did he do it?" The judge sees a family or social group striving to guide its children as normal families will; and the physician sees a child striving for independence as normal children will. The ultimate disposition of such problems rests in the hands of medically advised and socially trained judges.

DAVIDSON, Philadelphia.

INTERFERENCE THERAPY WITH COW POX VACCINE. N. BLATT, Wien. klin. Wchnschr. **42**:1255 (Sept. 26) 1929.

Blatt reports a case of syphilitic interstitial keratitis and one of keratitis eczematosa benefited by cowpox vaccination. He speaks of this as interference therapy and calls attention to other nervous and eye diseases greatly benefited by intercurrent diseases. In the broadest sense he also considers modern therapy, using organotherapy, protein therapy and colloidal therapy as interference measures.

BERENS, New York.

CEREBRAL CYSTICERCOSIS AND EOSINOPHILIA IN THE CEREBROSPINAL FLUID. CRISTOFORO RIZZO, Riv. di pat. nerv. **34**:936, 1930.

The author describes two cases in which a diagnosis of cerebral cysticercosis was made during life and verified at autopsy. In both instances the diagnosis was made by the presence of eosinophilia in the spinal fluid.

VINCIGUERRA, Elizabeth, N. J.

A NEW NEEDLE GUARD AND GUIDE FOR PARAVERTEBRAL NEURONE BLOCK INJECTIONS. ELIAS L. STERN, Am. J. M. Sc. **179**:385 (March) 1930.

A long needle, resembling a lumbar puncture needle, with an adjustable guard that can be moved away from the hub but not toward it, is presented for injections of the paravertebral nerve root. The procedure is simply described and offers a safe method for the injection of the nerve roots in various painful diseases.

MICHAELS, Detroit.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 24, 1930

C. A. PATTEN, M.D., *President, in the Chair*

MONOCULAR NYSTAGMUS. DR. A. M. ORNSTEEN.

A child, aged 10 months, born after a normal delivery and with no ailment previous to presentation, fell from a kitchen table to the floor without being rendered unconscious. A large swelling of the tissues developed above the left eye. No period of somnolence, unusual irritability or vomiting followed, and the child was apparently normal the next day. For two weeks the child was as well as usual, when suddenly one morning, it vomited repeatedly. That night it was restless and had a moderate rise of temperature. On the next day, the mother noticed a jerking movement of the head in the lateral direction. This had never been present before, and the child was not in the habit of vomiting. Within a few days, a rapid lateral oscillation of the right eye began; otherwise the baby appeared to be well. This condition had been present for two weeks when first observed at the University Clinic.

The nystagmus of the right eye was fine, very rapid and lateral. The left eye was motionless in a nystagmoid sense. The ophthalmoscope was used to make certain that the nystagmus was strictly unilateral; since often cases of so-called unilateral nystagmus are really bilateral, being more prominent in one eye, and in the other eye detectable only by observing the vessels in the fundus with the ophthalmoscope, when slight oscillations are noted. In this case this observation was negative. The nystagmoid movements in the right eye consisted of rapid oscillations of short amplitude lacking the alternating slow and quick components of organic nystagmus. Examination of the fundus was also negative for pathologic changes. There was an associated head nystagmus in the lateral direction with occasional rotary movements.

The first impulse on the part of the examiner was to consider these phenomena as posttraumatic. But the child was too well otherwise and a month had elapsed since the accident; besides, how and where could one localize a traumatic lesion, of necessity hemorrhage, to cause head nystagmus and monocular nystagmus? The thought of spasmus nutans had not occurred until it was seen referred to in several ophthalmologic textbooks. It then at once became apparent that this child was suffering from this disorder, which is occasionally an associated phenomenon of rickets. The head injury, two weeks before the onset, was a coincidental occurrence and was without causal relationship. The acute onset with vomiting and fever is probably akin to the onset of so-called acute rickets. Roentgenograms of the long bones, however, did not reveal the early signs of rickets. The child was teething and salivated freely.

Still, in his book, "Common Disorders and Diseases of Childhood," stated that the onset of this infection was often without apparent cause during the period of teething, preceded or followed by a period of head-nodding, but completely disappearing after a few weeks or months. Peter, in his book, "Extra-Ocular Muscles," referred to unilateral nystagmus as usually vertical, but stated also that it might be lateral and the movements rapid and of short amplitude. He also stated that the unilateral cases were rare except in spasmus nutans in children. H. Neuman, in "Die deutsche Klinik," referring to spasmus nutans or nictitans,

stated that the principal symptoms were tremor of the muscles of the neck and peculiar movements of the ocular muscles; nystagmus in one or both eyes (lateral, vertical or rotary). The nodding of the head may be anteroposterior or lateral. It has no connection with tetanoid hyperirritability of the nervous system. Nevertheless, its periodic appearance follows laws similar to the other forms of spasm in children. Thus among thirty-five cases, he observed thirty-one between December and April and only one in May, June, October and November, respectively. Complication with rachitis is not typical, therefore one may assume that the same deleterious effect of season, as in rickets, also favors the appearance of spasmus nutans as well as tetany. Nodding spasm may occur until the end of the third year, but is most frequent between the sixth and eighteenth months. The preponderance of females is conspicuous (twenty-eight girls to fifteen boys).

Oppenheim, in his textbook, stated that he had seen only two cases of unilateral nystagmus with spasmus nutans. Duand, in 1906, collected fifty-two published cases of unilateral nystagmus and divided them as follows: (A) with spasmus nutans; unilateral opacities in the media; (B) unilateral amblyopia and squint; unilateral high astigmatism; nervous diseases (?).

At the time of this report, the nodding spasm had disappeared and the nystagmus had become greatly lessened.

SUDDEN WHITENING OF THE HAIR AFTER MENTAL STRESS. DR. JOSEPH V. KLAUDER.

A man, aged 47, had always been of a nervous and high strung temperament. On examination, no neurologic abnormalities were present except exaggerated patellar reflexes. At the time of presentation he was almost completely bald. The few hairs that were present, were white. About two months before presentation, many areas of alopecia areata of the scalp appeared. These areas gradually enlarged and new areas appeared until almost all the hair fell out. Prior to the onset of alopecia there was no history of fright or emotional disturbance. He had been worried considerably about the behavior of his son.

In 1918, he was employed as a draftsman by a large ship-building company engaged in building ships for transporting troops in the World War. His work as a draftsman consisted of approving the drawings for the construction of these ships. He approved certain specifications which he should not have passed, allowing too close spacing of rivets in the iron plates which weakened them. These ships were later recalled from service and the faulty construction corrected. In the interval, however, the thought that these ships were not seaworthy tormented him. He was harrassed by the thought of their breaking up in midocean with a tremendous loss of life. He was blamed for passing these specifications and was threatened with criminal prosecution. He was unable to sleep for a week, ate very little and lost much weight. At the end of this period of worry he was called as a witness in an official investigation. The night of the day of this investigation he shaved before going to bed, as was his custom, and did not notice anything unusual about his hair. The next morning (he was away from home, living in a hotel) he did not know that his hair had changed color until he arrived at his office when fellow workers exclaimed with horror and amazement, "What is the matter with your hair, it is snow white."

Before the change of color of the hair, which was limited to the scalp, it had been dark brown. There was no alopecia.

At one time, considerable skepticism prevailed relative to observations that the hair might "turn white in a single night," but in recent times there has been ample confirmation of this observation. Vignolo-Lutati (*Policlinico* **25**:680, 1918), recorded instances in those engaged in front line service in the recent war. Landois (*Virchows Arch. f. path. Anat.* **35**:575, 1866) reported a case which he observed in a man aged 35, who was admitted to the hospital suffering with delirium tremens. The delirium took the form of great terror whenever any one approached

him. The well known case of Marie Antoinette may be mentioned. A number of other instances have been reported in perfectly healthy persons.

In some instances, the discolorations came over night; in others, in a few days, while in others, the period varied from a few days to a few weeks. In some instances the canities was associated with neuralgia-like pains and tender areas on the scalp. Canities of the eyebrow and eyelashes has been reported (Posey, *Tr. Coll. Phys. Phil.* **45**:335, 1923). The loss of color is alleged to be due to an infiltration of the hair with air.

DISCUSSION

DR. A. M. ORNSTEEN: I have nothing to offer in explanation of this disorder, but a case comes to my mind in which decolorization of the hair occurred in a short space of time. A woman, in her thirties, a brunette, received a telephone call at about 2 p. m. telling her that her child had just been run down by a truck and was in the hospital. When her husband returned home at 5:30 p. m., he observed that his wife's hair was snow white. He was certain that his wife's hair had been of its normal color at 9 a. m. that day when he left for business, and that there had been no graying hairs observed before this date. The patient was positive that the change came on during the hours between 2 and 5 p. m. The decolorization was complete.

It is stated that the chromaffin system is concerned with the distribution and fixation of pigment. The chromaffin system is an integral part of the sympathetic nervous system, which is intimately associated with emotional and psychic levels. It is possible that a sudden and severe psychic trauma produced a profound change in the metabolism of the chromaffin cells in the cortex of the suprarenal bodies through the sympathetic nervous system. As a result of this, a rapid decolorizing or bleaching process took place through biochemical changes in the pigment-bearing cells. This mechanism, I believe, is different from that of alopecia which does occur as a result of psychic trauma. This type of alopecia may be in the form of alopecia areata or universal alopecia.

SOME CONSIDERATIONS OF THE NEUROLOGIC CONDITIONS OF THE NEW-BORN. DR. CLARENCE A. PATTEN.

This paper, the annual address of the president, will be published in full elsewhere in the ARCHIVES.

PARTIAL UNILATERAL THORACIC GANGLIONECTOMY FOR RAYNAUD'S DISEASE WITH BILATERAL IMPROVEMENT. DR. TEMPLE FAY.

John M., aged 41, was admitted to the Neurosurgical Service of the Samaritan Hospital, on Nov. 20, 1929, having been referred by Dr. William A. Steel, with the chief complaint of swelling and ulceration of the remaining fingers of both hands, and excruciating burning and tingling sensations, with feelings of heat and cold in both hands. The patient stated that he had been well and active until eight years before presentation when he injured the great toe of his left foot. Following this, the foot became gangrenous and was amputated. Five years later, the fingers of the right hand became blue and swollen. There was a marked burning sensation in all the fingers, especially the little finger which was amputated at that time for gangrene. A year later, the right big toe became blue, swollen, painful and gangrenous; it also was amputated. Two years before presentation (November, 1928), both hands became painfully swollen and cyanotic and the fingers showed ulceration at the tips.

When admitted to the hospital, the patient was studied in the service of Dr. William G. Spiller. The fingers at that time felt as though they were on fire, and were so sensitive and painful that he could not use them.

It was the opinion of Dr. Spiller that the patient had Raynaud's disease. Dr. George Muller saw the patient in consultation and advised periarterial sympathectomy; the patient's symptoms in the lower extremities improved but those in his hands remained and the fingers began to ulcerate. At intervals of approximately one to two weeks, six fingers were removed. There remained the index finger and the thumb on the left hand and the thumb and ring finger on the right hand. The wounds healed gradually and the patient was discharged, improved especially in regard to the symptoms in the lower extremities.

Later, the remaining thumb and finger on the right hand were deeply cyanosed and ulcerated, and the nails sloughed away. The same condition existed in the left hand in the thumb and index finger. The patient could not bear even to have the bed clothes touch these remaining fingers. He kept them wrapped in gauze smeared with petrolatum and frequently held them out of the window to obtain relief from the constant burning sensation. It required morphine to bring sufficient relief from the distress for short periods of sleep. He stated that cold weather greatly increased the pain and begged for amputation of the hands to obtain relief.

Examination.—The patient was an undernourished man whose expression indicated constant torment from pain. The pulse at the wrist was barely perceptible. The blood pressure on the left was 110 systolic and 80 diastolic; on the right, 110 systolic and 60 diastolic. Only the following physical abnormalities were observed: there were dental caries; scars over the brachial and femoral vessels; loss of both great toes; loss of all fingers excepting the thumb and ring finger on the left hand and thumb and index finger on the right hand. The heart and renal functions were normal; a blood count revealed: red cells, 5,900,000; white cells, 7,600. A Wassermann test was negative. A blood culture gave negative results; a provocative Wassermann test gave 1 plus result; the blood sugar was 100 mg.; the nonprotein nitrogen, 40 mg.; uric acid, 4. Roentgen examination of the chest and spine gave negative results.

Neurologic Examination.—There was no cranial nerve disturbance. The pupils were round and regular, and responded promptly to light and in accommodation. The eye movements were full in all directions; there was no nystagmus. The visual fields were normal; the eyegrounds normal. The reflexes in the upper extremities were present, but slightly diminished. No Babinski reflex was obtained. Vibration, position and gnostic senses were normal throughout; pain and temperature senses were normal. There was hyperesthesia of the fingers and toes.

Operation.—A left second thoracic ganglionectomy was done by the Adson method on Dec. 13, 1929. Under gas and local anesthesia the second rib on the left at its articulation with the second thoracic vertebra was resected. The rib was isolated and the periosteum stripped. The transverse process of the second dorsal vertebra and the right attachment were resected. The dura was carefully protected and retracted laterally. The sympathetic chain was located, and a nerve hook passed around the chain just below the second sympathetic thoracic ganglion. At this point, straining on the part of the patient caused the bulging pleura to be torn by the sharp edges of the resected rib and an immediate massive collapse of the lung ensued. The patient became cyanotic, and the anesthetic was discontinued and replaced by oxygen. Great respiratory difficulty developed, and it was evident that the operation could not be continued.

The sympathetic chain isolated on the nerve hook was rapidly sectioned and an immediate wound closure accomplished so as to prevent further pneumothorax. Fifty cubic centimeters of 50 per cent dextrose was given intravenously, and pure oxygen administered intratracheally. A needle was introduced into the pleural cavity beyond the fifth rib and connected to a suction apparatus, so as to reduce the pneumothorax immediately after the wound closure. The patient was in a state of shock and was given 300 cc. of saline solution intravenously with 50 cc. more of 50 per cent dextrose solution. The respiratory difficulty subsided and the patient was returned to the ward in a fair condition. Immediately after the

period of shock, a roentgenogram was taken of the chest; it showed complete collapse of the entire left lung with displacement of the heart and contents of the mediastinum to the right.

Postoperative Observations.—The patient's condition improved gradually during the next three days and a roentgen examination, on Dec. 16, 1929, showed that the left lung had expanded to about one third of its normal capacity. Ten days later, the patient complained only of pain in the left lower part of the chest. The color in the fingers of both hands had returned to normal; the pain had entirely disappeared, and the ulceration showed signs of healing. Two weeks later, the patient was up and about the ward apparently normal, with no pain or paresthesia of the fingers of either hand. He used the fingers well, and picked up objects without discomfort. There was evident growth of the finger-nails.

One month following the operation, the patient had no complaint whatsoever. He was able to dress himself. He grasped the examiner's hand with great power in his remaining fingers. There was no cyanosis on either side. The hands were warm and without trace of the former condition. The radial pulse was obtained easily on both sides.

Six weeks following the operation, the patient was discharged, completely relieved of the former symptoms and with no demonstrable vasomotor disturbance of the upper extremities. He has gained in weight, sleeps soundly without morphine, and the nails of the four remaining fingers have returned to almost normal size.

Summary.—The case is presented because of the remarkable sequence of events following a partial unilateral sympathectomy. It was the operator's intention to follow the Adson technic not only of resecting the gray rami extending from the second thoracic ganglion on the left, but of later undertaking a similar procedure on the right. The course of events prevented completion of the operation on the left and subsequent recovery on the right side gave no indication for need of operation on the right. The question naturally arises as to why a bilateral improvement should occur; I can see no answer to this question, unless the massive collapse of the lung on the left and the partial collapse on the right in some way affected the sympathetic influences from the chain of ganglia which lie so close to the pleural surfaces.

DISCUSSION

DR. FRANCIS C. GRANT: This is an extremely interesting case. Were the reactions of temperature taken in this patient? It is important to determine the temperature index prior to operation because the prognosis for a successful operative result depends to a considerable extent on whether or not the temperature index is high or low.

I am not entirely in accord with the diagnosis of Raynaud's disease. The patient is a man. While the condition is symmetrical, nothing has been said concerning color changes in the affected extremities. Did the patient's fingers become blanched and then blue, with a subsequent flushing? Palpation of the radial arteries showed that the pulse seems markedly diminished. I was unable to obtain any pulsations in the region of the ulnar artery. These facts would suggest that the case is one of Buerger's rather than Raynaud's disease. However, the results in Buerger's disease are frequently as satisfactory, so that the indication for thoracic ganglionectomy is clear.

As far as a bilateral result following a unilateral section is concerned, based on the experience of others, it seems that this may be noted for a while at least, but is apparently only transient on the side not operated on. In order to determine accurately whether all the sympathetic fibers to the upper extremity were severed, the determination of the temperature index postoperatively was important. The satisfactory result obtained here, however, makes me believe that the sympathetic supply to the upper extremity had been completely interrupted.

DR. TEMPLE FAY: Unfortunately, we do not have the apparatus that is used at the Mayo Clinic. I do not believe that such an apparatus is available in Philadelphia. It is intricate and expensive; therefore, the temperature of the skin was not taken by thermocouples. The diagnosis of Raynaud's disease was made by Dr. Spiller and agreed to by Dr. Mueller. Dr. Steel, Dr. Winkelman and others had made this diagnosis, and the case history strongly suggested its certainty. The reason for this patient's recovery and relief is not clear; I am not able to explain why the operation benefited him. Only a partial sympathectomy was done on the left side of the gangliated chain without section of the gray rami, as advocated by Adson. Certainly the relief on the right side was unexpected. The patient is able now to use his remaining fingers and has no pain. Furthermore, there is active growth of the finger-nails and a decided change in color both of the fingers and the hand. When the patient came there was such circulatory disturbance that it seemed almost inevitable that amputation of the remaining fingers would be necessary. The relief of the condition is evident.

I saw several patients with Dr. Dowman, of Atlanta, with Dr. Adson at the Mayo Clinic. I have seen no other case of bilateral improvement from a unilateral operation and no case in which a severe collapse of the lung occurred as in this patient. The question arises as to how much the collapse of the lung had to do with the final result; the effect of the pleural pressure on the exposed sympathetic chain must be considered in the light of the results thus obtained.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 4, 1930

LOUIS CASAMAJOR, M.D., *President, in the Chair*

SUBARACHNOID HEMORRHAGE. DR. IRVING J. SANDS.

There is considerable difference of opinion as to what should be included under the heading of subarachnoid hemorrhage. I shall therefore present a series of thirty cases in which subarachnoid hemorrhage was encountered, and leave for your decision the logical classification of these disorders. The condition either is more readily recognized or is of greater frequency than in the past. Subarachnoid hemorrhage results from blood entering the subarachnoid space, escaping from blood vessels, from adjoining blood clots or from the ventricles. This results from (1) trauma, (2) arteriosclerotic degeneration of the vessel wall, (3) septic or infectious emboli, (4) congenital weakness of the vessel wall, (5) ruptured intracranial aneurysm, (6) intraventricular hemorrhage and (7) blood dyscrasias.

Clinically, the condition is recognized by the presence of meningeal irritation signs, such as cervical rigidity and a Kernig sign; bloody spinal fluid, which is uniformly discolored when collected in several test tubes and which does not clot on standing; mild leukocytosis and fever; compromise of certain parts of the nervous system producing neurologic signs, and symptoms referable to the etiologic disease process causing the hemorrhage.

In the traumatic group I had three patients, all of whom had had a blow on the head, definite disturbance of consciousness, certain neurologic signs caused by irritation and compression of the brain and cranial nerves, and a bloody spinal fluid. They recovered, but still complained of headache, dizziness and inability to resume work. I had a case of traumatic subarachnoid hemorrhage, following encephalography, which came to autopsy.

In the arteriosclerotic group I had seven cases; six of the patients recovered and one died, no autopsy being performed.

In the toxic and infectious group I had six cases, all with autopsy. Four were due to meningitis; one to thrombotic endocarditis and the last to chronic glomerular nephritis with acute exacerbations.

Four cases in the series could not be explained on any basis other than that of a congenital weakness of the vessel wall. In one, the disks were covered by large hemorrhages, which finally disappeared, the patient recovering and leaving the hospital; five days after leaving the institution, he died suddenly at home. The second patient also was discharged from the hospital; he died in a week after leaving the institution. The third recovered and when last seen was well; the fourth recovered from the subarachnoid hemorrhage and died several months later from agranulocytic angina; nothing was discovered at autopsy to explain the hemorrhage.

One patient had a typical case of subarachnoid hemorrhage; he presented signs of superior alternating paralysis, which could be best explained on the basis of a ruptured intracranial aneurysm. The patient recovered and was in good health when last observed.

There were five cases of intraventricular hemorrhage, all of which terminated fatally. In one of the patients the entire ventricular system was flooded with blood. Death was almost instantaneous. Yet, on postmortem examination, no free blood was found in the subarachnoid space. This case is presented as of unusual interest in that it illustrates the possibility of ventricular hemorrhage without subarachnoid bleeding. It may be explained on the basis of blood entering the fourth ventricle, causing edema in the inferior angle, obstructing the foramina of Magendie and of Luschka, and producing death before blood could enter the subarachnoid space.

My cases of blood dyscrasia included two of aplastic anemia, and one of purpura hemorrhagica which produced subarachnoid bleeding and which came to autopsy.

DISCUSSION

DR. J. H. GLOBUS: I think that Dr. Sands included in his group too many cases which do not belong to so-called spontaneous subarachnoid hemorrhage. His description of spontaneous subarachnoid hemorrhage was exceedingly well done. Most of us are familiar with that syndrome and usually limit it to hemorrhages confined to the subarachnoid space, which are due to a discoverable or undiscoverable aneurysm. The intraventricular hemorrhages, which are usually the result of erosion of large vessel channels in the brain, with bleeding into softened areas communicating with ventricular cavities from which the blood finally finds its way into the subarachnoid space, form another group, as do those showing massive softening, abscess formation and conditions definitely inflammatory in character which are not uncommonly associated with oozing of blood into the subarachnoid or subpial space. Since they, unlike the spontaneous subarachnoid hemorrhage, are not puzzling at all, it would be better, I think, to keep them out of the group and to limit the discussion to true subarachnoid hemorrhage.

DR. CHARLES DAVISON: Dr. Sands has presented an unusually large amount of material on subarachnoid hemorrhages. Some of the cases, especially the infectious-toxic group, have interested me greatly. I have seen a number of cases; one a case of a brain abscess, which was shown last year, of eighteen years' duration, with a subarachnoid hemorrhage on the opposite hemisphere. I have seen subarachnoid hemorrhages in a case of myelogenous leukemia, in one of multiple sclerosis and in one of basilar tuberculous meningitis in which one of the vessels at the base of the brain was eroded. In the infectious-toxic group of hemorrhages I think that there is more than a mere infection of the vessel walls. The vessels belong probably to the constitutional type of weak vessels which are easily affected by toxins or infections. If this were not true, one would see subarachnoid hemorrhages in prolonged infectious-toxic conditions more frequently.

DR. ARMANDO FERRARO: I agree with Dr. Globus in limiting the term subarachnoid hemorrhage; it should apply only to cases of spontaneous subarachnoid hemorrhage. It might be applied also in subarachnoid hemorrhages complicating other pathologic conditions, provided that the subarachnoid hemorrhage is considerable and manifests itself through clinical symptoms which might be somewhat correlated to this complicated factor. I am, for instance, skeptical as to the inclusion under subarachnoid hemorrhage of cases in which the hemorrhage is very limited and incidental, as, for instance, in the case of abscess of the brain presented by Dr. Sands, in which only a small patch of hemorrhage was disclosed.

Among the toxic-infectious conditions labeled subarachnoid hemorrhage by Dr. Sands, I was particularly interested in the case of measles. Meningitis and encephalitis may complicate the clinical course of measles; at the present time I am interested in the pathology of such a process, but I do not know of any case of subarachnoid hemorrhage reported in the literature as an accompaniment of measles.

Will Dr. Sands tell us if in his case there was a concomitant encephalitis process or if the subarachnoid hemorrhage was spontaneous, thus allowing one to add to the nervous complication of measles the possible occurrence of a subarachnoid hemorrhage?

DR. LOUIS CASAMAJOR: I was hoping Dr. Sands would speak of the pathology of that type of subarachnoid hemorrhage one sees now and then clinically, often in groups of cases: the subarachnoid hemorrhage that has no obvious cause, a sudden onset and a clinical picture of meningitis, and in which the large majority of patients recover. In the last four or five years I have seen probably fifteen cases; there was only one death. I recently saw a woman, about 50 years of age, who had had two attacks, the first one in 1926 or 1927, with a typical history of subarachnoid hemorrhage, sudden onset of severe headache, meningeal signs, a Kernig sign, and bloody spinal fluid, with a perfect recovery after four weeks. Following this she had a tendency to bleed from the nose at times. Last November, the tonsils were removed; following this there were severe ecchymoses beginning from the line of the chin and extending down over the neck onto the chest. Then in December, 1929, she had another attack of subarachnoid hemorrhage, with similar signs and apparently a complete recovery. When she was last seen there was nothing to indicate that the woman had ever had any meningeal inflammation or irritation. In 1926, and again recently, the coagulation time was not more than three minutes in a capillary tube. Hematologists in the Presbyterian Hospital were able to find nothing abnormal. The only suggestion they offered was that she probably had a purpuric tendency. Has Dr. Sands had any experience in cases of this sort?

DR. SANDS: From the literature I found that there was considerable difference of opinion regarding the types of cases that should be grouped under the heading of spontaneous subarachnoid hemorrhage. Many authors limited it to the group occurring in young people, as mentioned by Dr. Casamajor; some included cases following acute infectious diseases, while a still larger number included aneurysms and ventricular hemorrhage cases.

I was not able to read the records of all my cases, but shall publish them in full. In one patient there was a clear case of purpura hemorrhagica, and subarachnoid hemorrhage developed. Another patient who was treated for subarachnoid hemorrhage and who was discharged as cured, was later readmitted to the hospital and died from agranulocytic angina; at postmortem examination the brain showed a thickened fibroblastica pia, but no other changes.

I was particularly anxious to present the three cases of traumatic subarachnoid hemorrhage; they represent a number of patients who are not receiving the consideration that they deserve. The patients are examined years after the initial injury, and because at that time no neurologic signs are elicited they are called malingerers or litigating neurotics.

EXPERIMENTAL REMOVAL OF THE CEREBELLUM IN PART OR IN TOTO: A PRELIMINARY REPORT ON CEREBELLAR LOCALIZATION (illustrated with moving pictures). DR. ARMANDO FERRARO and DR. LEO M. DAVIDOFF.

The authors have experimentally removed various areas of the cerebellum, either of the hemispheres or of the vermis. The investigation dealt with various aspects of the importance of the cerebellum in the control of motility. In connection with this, the authors are also experimenting, among other things, on the action of bulbocapnine in normal as well as in partially or totally acerebellar animals.

From an anatomic standpoint, the authors are studying the correlations between the various pontile nuclei and the different lobes of the cerebellum. A report of these studies will follow later.

The data reported at this time dealt exclusively with the problem of cerebellar localization. The conclusions reached following a first series of numerous operations on cats are: The lateral lobe of the cerebellum controls the synergia as a whole of the muscles of the homolateral portion of the body. No bilateral control seems to exist. Of the lateral lobe, the lobus paramedianus seems to possess a more specific synergic control of both fore and hind legs of the same side, the area controlling the fore leg being located frontally to the area controlling the hind one. The removal of the lobus simplex is not followed by permanent appreciable involvement of the synergia of the body or of the head. The lateral portion of the anterior lobe (lobulus IV lateralis) seems to participate also in the synergic control of the muscles of the homolateral side.

In the vermis one may distinguish one area for the synergic control of the muscles of the neck, located in the culmen; one area for the synergic control of the anterior muscles of the trunk and of the shoulder girdle, located in the clivus, folium cacuminis and part of the tuber valvulae (lobus C II vermalis presulcal and postsulcal of Riley), and one very important area for the synergic control of the posterior portion of the trunk and for the pelvic girdle, located in the tuber, the pyramis, the uvula, and the nodulus (lobus A B C I and C II postsulcal of Riley).

The most important synergic control exercised by the cerebellum in the cat is the one over the hind portion of the trunk.

These conclusions are tentative only, as they result from work already done. They might be subject to modification in the ultimate course of further investigations.

DISCUSSION

DR. F. H. PIKE (by invitation): My own interest in the cerebellum has not been primarily that of localization. It is more in what the cerebellum does and in what part of it is concerned in that particular reaction. Concerning localization, I have been skeptical. I think one should be very cautious in presenting any criticisms, either commendatory or adverse, particularly adverse, at this time. The data seem conflicting. One observer reports that on stimulation of a definite region he gets definite results. His results may not be quite those that are postulated from the direct anatomic data. There is still, I think, some element which we do not quite grasp entering into this question of localization. For that reason I feel reluctant to express any opinion just now.

What I am interested in is the relation of these various portions of the cerebellum to the pontile nuclei, and I am interested also in the source of the afferent impulses that go into the cerebellum. Just as showing some of the elements in confusion which may enter here, one might imagine that if the dorsal roots of the spinal nerves from a limb were divided, there would not be much cerebellar control exercised over that limb directly. All the afferents from that limb are now eliminated. I was rather surprised to see in such an animal a recurrence of the original symptoms from a lesion of the lateral lobe of the cerebellum. I do not see what it means. That is, after the animal had begun to walk around well, using the hind leg the dorsal roots of which had been divided, a lesion of the lateral lobe of the cerebellum apparently was followed by a return of symptoms in that

hind leg as well as by symptoms in the fore leg. Apparently, the lateral lobe of the cerebellum controlled the movements of the fore and hind limbs of that side, even though all the afferents from one were eliminated. I do not see just what that means. That is just one of the things which makes me hesitate to say all that I think about this localization, or to express much opinion either way. It would look as thought there were something in the cerebellum that is concerned with associated movements of the limbs. However, I have not yet enough data to say much about that either.

The question of the relation to catalepsy and the action of drugs interests me considerably. I have made the observation that in recent injuries of the cerebellum of accidental origin, there is a real difference in the strength of the convulsions of the two sides of the body due to absinthe. One would suppose that absinthe would act about equally on the motor areas of the two sides or whatever else it does act on, but that in a recent unilateral injury of the cerebellum the animal would turn over rapidly and continuously to one side, whereas it does not do so when the cerebellum is intact. Even in movements of a convulsive origin, the cerebellum seems to have some effect on the strength of the contractions.

The question of compensation for cerebellar injuries is another thing. I do not believe that much was said of shock or inhibition; I do not remember that Dr. Ferraro mentioned either one tonight. Shock and inhibition seem to be stock articles in trade when knowledge fails, but I do not think that one adds much by using two terms of which one knows little.

Tremor of the head is often one of the last things to disappear after cerebellar injury, and that comes on only when the animal is looking at one intently. I do not wonder that Dr. Ferraro was not able to bring it out in the moving pictures; one has to look intently to observe it. It is a fine tremor, and may be the last thing which persists. As to why it disappears, I have two suppositions. Something else in the cerebellum has taken over that function, or some associated structure is concerned in it. I have found that after complete recovery from a lesion of the vermis in an animal in which this fine tremor of the head was the only remaining symptom, a lesion in both internal ears was followed by a return of the swaying movements of the head which were prominent and lasted as long as the animal lived. This is not the usual effect of removal of both internal ears, and I do not believe that one would argue from this that the main central channel from the vestibule lies through the cerebellum. Obviously, a pathway that is broken up by a cerebellar lesion would scarcely cause a recrudescence of symptoms when its end-organs are destroyed.

I envy Dr. Ferraro the grass and sunlight for his cats, because they do much better when they have grass and sunlight than when they are kept in closed rooms, no matter how much the aggregation of bricks may have cost.

Dr. Henry Alsop Riley: I think that Dr. Ferraro has been much more kind than accurate in his remarks as to what he terms "my" nomenclature, because it is not my nomenclature; practically 95 per cent of it is Bolk's nomenclature, which I hope may be used in the description not only of experimental but also of pathologic and anatomic discussions of the cerebellum. I think that there can be no question but that the use by Dr. Ferraro of the simplified nomenclature in his consideration of the caudal lobe made his discussion much more intelligible than other presentations which have consisted largely of a string of names such as the lobulus gracilis, the lobus biventer, the lobulus postero-inferior, the lunate lobule, the uvula, the tonsil, etc., until one scarcely knew which part of the cerebellum was being described. It is probably because I am more familiar with comparative terms that it seems to me this simplification and unification of cerebellar nomenclature is well worth while; if it is continued, conversation in regard to the cerebellum will be much more intelligible than it has been in the past. I sincerely hope that Dr. Ferraro will gradually eliminate the lingula, the culmen, the lobulus centralis, etc., and use the term I. II, and IV, C, B, and A which are so much easier to remember.

In regard to any attempt at localization at the present time from the moving pictures and the records of his operation, I hope that Dr. Ferraro will not come to too definite conclusions before autopsy is performed and the anatomic preparations are carefully examined. In particular, I think it important that careful examination of the stem should be made in order not to complicate the picture with symptoms that may be due to lesions of the tegmentum or the basis, and which are not strictly referable to the operative lesions in the cerebellum. Two conclusions that he has mentioned in regard to localization interest me greatly. The first one is that connected with the vermis, which for a long time has been considered to be chiefly connected with the synergy of the trunk and the bilaterally innervated musculature; this has received confirmation from Dr. Ferraro's work and is in more or less direct line with the conclusions which were reached in my study of the comparative cerebella, in which the vermis was very much more extensive in large bodied animals, particularly the ungulates in which the musculature of the axial column is so great. As I mentioned in my description of the comparative cerebellum, this demand of the axial muscles for synergy is so great that in some of the forms one finds an actual paravermis, that is, a budding-out or spreading-out of the vermis, which would appear to casual inspection to be a part of the hemisphere, but which is in reality an integral part of the vermis.

The other point that interested me concerned the lobulus simplex, which has been considered to control the synergy of the musculature of the neck. This fact I was not able to corroborate, and in Dr. Ferraro's experiments he reaches apparently the same conclusions to which I finally came, that in all probability lobulus 4 is more closely connected with the synergy of the neck than is the lobulus simplex. In my work, I found the lobulus simplex to be extremely variable; it was merely an anatomic arrangement of a few folia of cerebellar tissue which have no constancy in any of the groups examined.

I wish also to speak of the extremely good condition of the animals. I do not think that I have ever seen a group of laboratory animals in which the physical condition was so uniformly good; this speaks volumes, not only for Dr. Ferraro's supervision, but also for the technical assistance which he has in the Psychiatric Institute. I think that the presentation is an admirable example of the value of moving pictures in research, particularly neurologic research.

DR. DAVIDOFF: I have relatively little to add; I wish only to reemphasize that we are presenting tentative conclusions of work which is still in progress. Moreover, we have so far been able to present data only on a single species of animal; we hope to carry out the work on other species, particularly on monkeys. I do think that we can say that the localization of coordinated function of the trunk muscles in the vermis is fairly well established, not merely from our work, but because our work confirms the work of so many others, including Dr. Riley's comparative anatomic studies. In spite of the indefiniteness of our conclusions, it nevertheless raises analogies to clinical conditions; there, too, the same confirmation of the control of the body musculature by the vermis appears. Perhaps the most common lesion of the cerebellum to be seen by the neurosurgeon is a tumor of the cerebellum in young children, usually confined largely to the vermis. These cases will show practically no nystagmus, and in bed the patient has excellent coordination of the muscles of the arms and legs. In walking the patients have a wide base; they tend to fall in either direction, and they have a definite loss of equilibrium. This is again emphasized, and perhaps even better, when these children are placed on the floor to walk on hands and knees like quadrupeds. They then show the same swaying of the body from side to side and the peculiar dissociation between the anterior and posterior parts of the body, as if there were a joint somewhere in the middle of the trunk over which they seem to have no control, exactly like the cats demonstrated on the screen.

DR. FERRARO: I wish also to emphasize that our conclusions are only tentative. They will certainly be modified in the ultimate course of the work if the collection of new data does not substantiate our first results.

The problem of localization is such an important one that we are justified in enlarging as much as possible the field of investigation. With the cooperation of the Psychiatric Institute, which has already given us the facilities for this work, we shall continue the investigation. We also hope to be in a position soon to report on the anatomic data in which Dr. Pike is especially interested, concerning the important connection between the cerebellum and the various pontile nuclei.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, Feb. 11, 1930

MOSES KESCHNER, M.D., *President, in the Chair*

ACUTE HEMORRHAGIC LEPTOMENINGITIS. DR. IRVING PARDEE.

Two patients presented the following clinical picture: Sudden onset of disturbance of consciousness and confusion, stiffness of the neck, contracted sluggish pupils and retinal hemorrhages with some blurring of the margins of the disks. The reflexes were exaggerated, and there was a positive Kernig sign; the temperature was between 99 and 101 F. The outstanding complaint was headache, severe and persistent, with occasional nausea and vomiting at the onset. The spinal fluid was uniformly bloody, gradually clearing as the patient recovered, and showed a lymphocytosis associated with an increase of protein and many red blood cells.

This syndrome indicates an involvement of the meninges with a hemorrhagic process, in which there is fever and a definite inflammatory reaction in the spinal fluid. These patients were suffering from an acute inflammation of the leptomeninges in which there was a tendency to hemorrhage. It is my belief that this clinical picture can be separated from the main group of cases heretofore called subarachnoid hemorrhages. The latter name is inclusive, and it seems that a variable etiology can be found for different forms of subarachnoid hemorrhage. One form is the type presented by these patients; it can be split off from the main group and made a separate clinical entity, namely, an acute leptomeningitis, hemorrhagic in type.

DISCUSSION

DR. FOSTER KENNEDY: When I heard Dr. Pardee's narration, I thought that he was describing an aneurysm within the skull. I am not sure, unless he has had an opportunity to follow the cases for a considerable time, say two years, that they are not cases of intracranial aneurysm. Such episodes have been observed two and three times before a fatal hemorrhage has occurred, as the result of an aneurysm of one of the larger cerebral vessels.

On the other hand, were it not for the fact that he uniformly found blood in the cerebrospinal fluid, I would think that his cases corresponded with some that I observed six or more years ago; they were described under the heading of acute meningo-encephalitis with papilledema. There was a very acute onset of unconsciousness and meningeal signs, and usually considerable disorientation of the mind. There were some fever, pleocytosis in the spinal fluid, but no blood, and usually some localized cerebral insult such as a hemianopia, a hemiplegia or a monoplegia. Within two or three weeks after the illness began, the papilledema always cleared up, having been exceedingly severe for two or three weeks. The papilledema was undoubtedly due to an acute hydrocephalus, caused perhaps by an ependymitis that produced dilatation of the ventricular system. All of the patients recovered, so that there was no opportunity to explore the intracranial pathologic changes.

My principal difficulty in understanding Dr. Pardee's story is as to how he was able to be sure that there was a lymphocytosis in the spinal fluid in the presence of as much blood as he described.

DR. IRVING PARDEE: I purposely did not review the extensive literature on this subject. I did not wish to present a paper; I wanted merely to report the two cases. In them I found no evidence of arterial disease which would lead me to suspect an intracranial aneurysm. The more I think over the cases and the clinical course, the more do I believe that the condition was an inflammatory rather than an exudative or a hemorrhagic process.

First, the changes in the eyes, as reported by Dr. Johnson, were considered by him to be definitely toxic or infectious. Second, the spinal fluid, which was studied by Dr. Hillman, should, if this were a hemorrhagic process, present a polymorphonuclear increase in some way comparable to that of the blood. Yet, all of the examinations of the spinal fluid showed a lymphocytosis. The original specimens, although very bloody, did not clot; they were therefore susceptible of detailed analysis as to the type of cells present.

I cannot believe, as I have already said, that these are cases of a form of encephalitis. Many years ago, Dr. W. M. Kraus and I studied the spinal fluids in about 250 cases of encephalitis; we found no evidence of a bloody fluid, although there was frequently a lymphocytosis.

THE VALUE OF ENCEPHALOGRAPHY IN THE DIAGNOSIS OF INTRACRANIAL LESIONS. DR. CHARLES H. FRAZIER.

My experience with encephalography is included for the most part within the past three years; during this time I have sent much material from my service to the x-ray department. Much of this material has already been used in demonstrations of one kind or another by the x-ray Staff. I shall confine my remarks to the value of the encephalogram to the clinical neurologist or neurosurgeon in the interpretation of certain clinical pictures. I wish to emphasize a point in the technic of encephalography which contributes to the patient's greater comfort. It was not until this technic was adopted that I consented to subject patients to the injection of air by the lumbar route. If the fluid is withdrawn slowly and in small amounts, not more than 5 cc. at a time, and the air is injected slowly in equal amounts, never injecting more air than the fluid withdrawn, the degree of discomfort is reduced to a surprising degree.

The cases selected for illustration (with lantern slides) fall into three groups: (1) the late effects of grave cerebral trauma; (2) essential and traumatic epilepsy, and (3) suspected tumor of the brain.

(1) A number of patients are referred to the Neurosurgical Service months, perhaps years, after a grave cerebral injury. The common sequelae are vertigo, tinnitus, headache, memory defects, etc. Many of these have been treated as neuroses. In this series not only have I invariably found some abnormality, but the picture has been surprisingly constant, in some more exaggerated than in others. The picture includes enlargement of the sulci over one or both hemispheres, and dilatation of one or both ventricles, the ventricle on the side of the damaged hemisphere always being the larger. I interpret theses abnormalities as signifying a definite shrinkage or atrophy of one or both cerebral hemispheres; in many cases there is evidence of corresponding shrinkage of the cerebellar hemispheres. In 10 per cent the lateral ventricle failed to fill, indicating a valvelike obstruction to the ingress of air.

This observation has great importance in medicolegal cases. If it is not possible to eliminate malingering, one can at least say, should the encephalogram reveal a picture as described, that there were grave structural changes of traumatic origin in the brain mass.

(2) In the group of traumatic epilepsies the picture did not differ materially from that described in the traumatic series. Even in the so-called essential epilepsies there is a surprisingly large number of cases with definite abnormalities,

most often characterized by an enlargement of the cerebrospinal fluid pathways. In addition, in certain cases there were large porencephalic cysts communicating with the lateral ventricles. The similarity of the observations in the cases of postraumatic and essential epilepsy led me to suspect that many of the latter may have been the result of an unrecognized birth or postnatal trauma.

(3) Caution must be exercised in resorting to encephalography in suspected brain tumors; I employ it only when the cerebrospinal fluid pressure is not more than 200 mm. of water. Obviously, in the presence of increased pressure one fails to find air in the subarachnoid spaces over the cerebral hemispheres. Except in midline tumors, the third, fourth and lateral ventricles are easily visualized. In many cases a localization has been established. In a few cases, usually midline tumors, no air was seen in the fourth, third or lateral ventricles; under such circumstances I have had to follow the encephalogram later with a ventriculogram. I believe that in cases of suspected tumor of the brain the encephalogram has served a greater purpose in excluding tumor and thus avoiding the necessity of an exploratory operation.

The encephalogram possesses advantages over the ventriculogram, especially in that the former avoids the necessity of an incision and perforation of the skull. The encephalogram as employed in my clinic has proved safe. In the total series of 140 cases there have been no fatalities. I am inclined to think that in the past encephalography has been resorted to more frequently than it will be in the future. At the same time I am convinced that this procedure serves a definite purpose and will prove of great assistance in selected cases.

DISCUSSION

DR. FOSTER KENNEDY: I have had the pleasure of watching Dr. Charles Frazier at work for approximately twenty years; always I have been struck by his having been constantly in the forefront of the battle. When any step is taken in diagnosis or therapeutics, Charles Frazier is sure to be there. In regard to the addition to our armamentarium which he has discussed in this paper, he has shown again that he is well aware of its advantages and has made use of them.

In New York we have been perhaps a little more conservative than you have in Philadelphia. We are more afraid, I think, of doing encephalograms in cases in which a tumor is suspected. I believe that encephalography by the lumbar route is the ideal method for exploration of the subarachnoid spaces when the pressure is not raised. In cases of lesions of the midbrain and of the posterior fossa, I am inclined not to risk it, as I have observed cyanosis, serious collapse and, in one case, death. For that reason I was surprised to hear that Dr. Frazier made an encephalogram in a case in which he said an angle tumor was suspected. In that type of tumor I am afraid to risk this procedure. I do not doubt that Dr. Frazier can give a good reason, but I am inclined to criticize the procedure of making encephalograms with a pressure of 200 cc. in the case of a cystic tumor of the motor zone. I do not believe that one should use this method, valuable as it is, until one has exhausted completely the clinical armamentarium. There is also a philosophic reason for that; one is in constant danger of being led by the nose by mechanical procedures and losing the "Sydenham touch," becoming unable to detect crepitus in a fracture because the x-ray picture shows the bone, and unable to use our own brains because one can see the other fellow's with the use of the x-ray pictures.

In my opinion, Dr. Frazier has made an important contribution in the series of plates of what he calls essential epilepsy. Birth is certainly the most hazardous adventure of life. Recently, Carruthers subjected 100 new-born infants to lumbar puncture and found free blood in the spinal fluid of fourteen, 14 per cent of cases in which there were no symptoms. I do not doubt that subarachnoid hemorrhage in the infant produces microscopic changes which deform the brain, interfere with the blood supply and lay down the mechanism, by interference with the blood supply of cerebral excitable tissue, for future epilepsy. Dr. Frazier's encephalo-

grams, corresponding with those taken in New York, show that in a fair number of epileptic patients, without demonstrable neurologic signs of structural deterioration, there are structural abnormalities which probably lie at the basis of the convulsions.

I wish that Dr. Frazier would define what he means by severe cerebral trauma as producing deformities of the brain substance. Experience in New York and also in Germany, like that of Dr. Frazier, has been that after cerebral injury changes are found in the shape and size of the ventricles and in the size of the subarachnoid space; it is extremely important, however, from a medicolegal point of view, that one has, as Dr. Frazier says, a clear idea of the normal ventricle and subarachnoid space. A great many psychoneurotic persons have suffered from minor injuries, and the symptoms occurring from these injuries are the same as those occurring from major injuries. It is important to know in what cases an encephalogram is justified, and how much trauma is necessary to produce changes in structure such as are seen in the encephalogram.

Dr. Emanuel D. Friedman: I can only echo the sentiments expressed by Dr. Kennedy concerning Dr. Frazier's important contributions to clinical neurology and this excellent paper. I shall confine my remarks to a few points. In contrast to the statement concerning the inadvisability of carrying out encephalography in cases of brain tumor, I would say that the existence of a cerebral new growth is no contraindication to encephalography, even when the intracranial pressure is slightly elevated. In a series of nearly sixty cases of neoplasm at Bellevue Hospital, we have had two or three fatalities, it is true, but in the others we have obtained a great deal of information, valuable to us and to the operating surgeon. I believe that in carrying out encephalography in cases of brain tumor one should be more careful than in instances in which there is no increase in intracranial pressure. One should make certain that the fluid is withdrawn slowly, and that no bubbles of air issue from the mouth of the tube while the fluid is escaping. When about 70 cc. has been injected and the patient shows evidence of syncope, one should stop and allow the circulation to reestablish itself; one may later inject a volume of air sufficient to be visualized on the plates. In cases with papilledema one should inject not more than from 70 to 80 cc. of air (we usually inject from 100 to 110 cc.). We have obtained satisfactory plates with quantities varying from 75 to 90 cc.

I believe that the only contraindication to encephalography is the existence or suspicion of tumor in the posterior fossa. The insufflation of air must be performed with the patient in the erect posture; the escape of fluid from the subarachnoid space exposes a patient with a tumor of the posterior fossa to the danger of herniation of the cerebellum into the foramen magnum and medullary death. I think, too, that, generally speaking, encephalography is a safer procedure than ventriculography, although the technic recently developed by Dr. Frazier and his pupils lessens the danger of the trephine method. Most observers have found that the mortality from encephalography is much less than that from ventriculography.

I wish to stress also what Dr. Kennedy said concerning the "Sydenham touch." It is necessary that one should try to arrive at a clinical diagnosis before subjecting any patient to the procedure of encephalography. Nevertheless, in certain cases clinical acumen fails; one must therefore employ every means at his disposal or he will fail to make an exact diagnosis.

The after-effects of encephalography are frequently severe, especially the headache; in most cases this symptom can be ameliorated by the administration of hyoscine and morphine and by immobilization of the head; the headache is often no worse than that observed following lumbar puncture.

The nonvisualization of the ventricles in certain cases of which Dr. Frazier has spoken occurs sufficiently frequently to make it noteworthy; there is as yet no adequate explanation for the failure of the air to reach the ventricles. Monakow believes that the foramina of Magendie and Luschka are only potential fora-

mina; they may therefore permit cerebrospinal fluid to escape, but, acting as ball-valves, may block the entrance of air into the fourth ventricle.

I think that Dr. Frazier has shown a few instances in which encephalography may be extremely valuable. It is valuable for the precise localization of tumors. In most cases of tumor one finds the ventricle, on the side opposite to the lesion, dilated, and that on the same side diminished in size or not visible. Dr. Frazier has shown in one of his plates that the homolateral ventricle was larger than the one on the opposite side. This is noted in cases of neoplasm occupying a position high up in the hemisphere. In such cases the contralateral ventricle is frequently elongated and distorted, and there is often no ventricular shift.

Of course, the encephalogram is extremely valuable in the differential diagnosis of vascular or degenerative disease from neoplasm, particularly in cases in which there is no papilledema. Patients who have reached the time of life when vascular crises or accidents occur may go many months with intermittent convulsive seizures and later pareses may develop. The clinician is unable to determine whether he is dealing with an expanding lesion or a vascular degeneration. Here encephalography has achieved its greatest value. A ventricular shift to the side opposite to the lesion, obliquity of the third ventricle and dilatation of the contralateral ventricle speak definitely in favor of a new growth, even in the absence of papilledema. In cases of vascular or degenerative disease, on the other hand, the ventricular dilatation occurs on the side of the lesion and the ventricular system tends to migrate toward the diseased side. This picture has been called hydrocephalus ex vacuo by Foerster.

The encephalographic observations in traumatic neuroses and the epilepsies are similar to those observed in vascular and degenerative lesions of the brain. One might, therefore, postulate a common underlying factor in the traumatic neuroses and the epilepsies, namely, necrobiotic disturbances secondary to vasomotor changes such as have been described recently by Spielmeyer. Incidentally, I might add that encephalography is well borne in all instances of degenerative disease of the brain.

Our experience now covers a period of well over three years, and the number of our encephalographies has grown to more than 200. It is my belief that encephalography has come to stay and that it should be incorporated in the diagnostic armamentarium of every neurologic clinic.

DR. MICHAEL OSNATO: A word of caution is necessary. I refer particularly to the interpretations of the traumatic point of view in the cases of epilepsy studied by encephalography. In the first place, I fail to see that any convincing demonstration has been made of what is the normal encephalographic picture from studies made of healthy persons when subjected to this measure. Secondly, I should have liked to have heard from roentgenologists something more about the possible errors of interpretation due to the inherent difficulties that apply as to filling and distribution of air in a considerable group of normal patients who complain only of non-neurologic situations. That is a problem not for the clinician or the neurologist, but for an expert x-ray physicist.

The third point is the great danger of describing in old epileptic patients who have had severe seizures, with injuries to the head during many seizures, the structural changes shown in the plates as the primary factor in the epilepsy. I think, on the contrary, that such evidence as we possess would tend to indicate that the defects in these plates, if such, are secondary and not primary. In the work done on old epileptic patients on Ward's Island by Dr. Notkin, the results would seem to confirm Dr. Frazier's observations; but these were old, severely chronic psychiatric patients, many of whom have been in status. I think that one should be very careful in assuming that the observations are the primary cause of the epilepsy for one knows that trauma can be only one of a number of factors.

Finally, I shall call attention to the English survey of craniocerebral defects growing out of the World War. Of 25,000 patients, only 4 per cent developed craniocerebral defects. The survey was completed about six years after the injury.

Dr. William Snow: From the standpoint of the roentgenologist, I may say that we are dealing with a difficult technical problem. Because of the structure of the ventricular system, particularly because of the fact that the ventricles communicate with each other by rather small channels, it is impossible to replace with air all of the fluid within it. For this reason, in order to outline with air the various parts of the system, the head has to be shifted for the different radiograms. Coupled with this is the fact that the patients do not cooperate well. They have terrific headache and are often sick as a result of the injection of air. Many are not normal mentally. It is a problem to keep the patient placed properly. If, however, the radiography is carried out carefully by someone who understands the problem, the results are reliable, permitting of fairly accurate interpretation.

I noticed from Dr. Frazier's slides that all views were taken with the patient in the erect posture. At Mount Sinai Hospital, New York, we have followed the procedure of examining the patient in the prone as well as in the erect position. I think that it is more advantageous to use both, because the descending horns, being the most dependent part of the system, do not fill with air when the patient is erect.

Has Dr. Frazier had any experience in performing encephalograms in patients who have the condition called "punch drunk" as observed in prize fighters? I think that it is important and that much light can be shed on it by encephalography. We have had no experience with them, but I imagine that these patients would show changes similar to those seen in posttraumatic headache.

Dr. Charles H. Frazier: Dr. Kennedy asked what I mean by severe cerebral trauma. One may learn from the history that the patient had an injury to the head, but one must inquire into the nature of it. He may have had a fracture of the skull; possibly yes, possibly no. We ask, "Were you hospitalized, and for how long?" He may answer, "Ten days" or "Two weeks." "Were you unconscious, and for how long?" He may answer that he was unconscious for a few days, a week or longer. If he was hospitalized for ten days or two weeks, and was unconscious for several days or longer, one may assume that the trauma was severe, either a massive hemorrhage or a severe contusion.

Dr. Kennedy took exception to encephalography in the cases of angle tumor; properly, in certain circumstances; but in all the cases of angle tumor in which an encephalogram was employed the pressure was normal and we knew that there was no risk of herniation. Furthermore, our encephalograms are made at about 8.30 a. m. in the operating room. From there the patient goes with the operator to the x-ray department. The films are developed immediately and within from fifteen to thirty minutes the operator sees the films and an immediate diagnosis is made. Should the diagnosis be tumor, the cranial exploration begins at once. Thus the risks from the injection of air in cases of brain tumor have been eliminated. The same procedure is followed with the ventriculogram. The patient is returned immediately from the x-ray department to the operating room, and if the diagnosis and localization are established operation is not delayed a moment. If these precautions are taken, there are no risks. I think that sometimes I may have been too bold in the freedom with which I have been doing encephalograms. I would not think, however, of making an injection of air in a patient suspected of having a tumor were the operating room and the operator not ready for immediate service.

Dr. Kennedy also took exception to my doing an encephalogram in a patient in whose case the localization was reasonably established by the symptoms. Suppose one has a patient with signs of a lesion of the motor cortex. The greater

portion of the tumor may be behind or well in advance of the motor cortex. If one makes the middle of the flap the rolandic fissure, he is either too far in front or too far behind. One should have the most exact information available in all explorations for tumor, not only as to the location of the tumor with relation to the cortex but, in subcortical growths, with relation to the ventricles.

To my mind, the most pertinent question asked was "What is a normal picture?" This is a perfectly proper question, but unfortunately we are unable at the present time to say with reasonable assurance what constitutes a normal picture and what an abnormal picture of the fluid spaces and pathways. We are handicapped by the obvious lack of normal cases in our clinical studies. We should know by actual measurement with the millimeter scale what is an enlarged cistern and what is an enlarged cortical pathway. That information is not now available. Wide deviations from what one presumes to be normal are, of course, readily recognized. Finer distinctions are still a matter of speculation.

It is true that in most instances the patients are very uncomfortable for a day or two. In some cases, however, the patients are extraordinarily free from discomfort. In making rounds in the early afternoon of the day on which the encephalogram was made, I have found a patient surprisingly comfortable; but many are nauseated; in many headache is intense, and for several days the patients should keep absolutely quiet. The slightest movement of the head to one side or the other causes a shift of air pockets and an aggravation of the symptoms.

I do not know what is the cause of symptomatic improvement following the injection of air. I mentioned Dr. Penfield's explanation because I have none of my own and do not know of any other. While the explanation remains obscure, nevertheless it is an observed fact that many of these patients are benefited.

I have had no experience with the so-called "punch-drunk" in encephalography.

MOVING PICTURES OF NEUROLOGIC CASES FROM MONTEFIORE HOSPITAL. (SYNCHRONIZATION BY THE RADIO CORPORATION OF AMERICA). DR. S. PHILIP GOODHART.

The moving picture is no longer a novelty, but a demonstration for study in medicine and surgery. It has become a part of the equipment of the hospital. The purpose of my presentation is first to demonstrate especially the value ot motion picture photography as a means of recording the clinical history of the progress of patients with deformities of motion, and thus, if necessary, to correlate the clinical pictures with determined pathology, and more particularly to emphasize the usefulness in medicine of the latest achievement in popular entertainment and instruction, namely, synchronization.

I hope that very soon we shall be able to show on the screen patients with language and speech defects, correlating the physical defects with their defective vocalization, as for example, in stammering, bulbar palsy, dementia paralytica, disseminated sclerosis and paralysis agitans. The advantages of such types for instruction and study are apparent.

There will be shown presently on the screen the value of obtaining on one film both the clinical picture and the vocal record of description, just as one hears it when the demonstrator is present in person. It is far easier to speak once in record, as I have done here, and thus have on a single film for permanent record a description that obviates the need of time and travel. The film alone carries at once the patient and the demonstrator.

The screen cases to be shown are almost entirely from the neurologic wards of the Montefiore Hospital. They have been shown previously, but are again selected from our library of films for illustrating synchronization.

The first case depicted shows the scenes of earlier history, in 1921, by Dr. Tilney and myself before the American Neurological Association. This case was then presented as one of psychogenic origin. I shall not now attempt to discuss it; the nature is gradually unfolded on the screen. Just a word as to its interest for diagnosis: The question arises as to whether the case was originally of

organic nature, or whether the patient suffered from a profound psychoneurosis expressing itself in motor symbolism, and that following this an organic disease, dystonia musculorum, developed independently of the previous psychomotor condition, or whether from the latter the organic condition developed, or whether the elements of both were originally present.

In presenting this case and others of organic nature studied by bradykinetic analysis, Dr. Tilney and I suggested that the posing and attitudinizing, so striking in certain well recognized organic diseases, seem to impress one with the close anatomic relation of these symbolic movements to the basal ganglia of the forebrain. The thalamus and the corpus striatum, which are functionally associated with sensorimotor complexes, serve as the centers especially controlling automatic associated acts and attitudes expressing the fundamental emotions; it is quite probable that such attitudes as express emotional states in true hysteria, or rather psychogenic states, may have their subconscious and anatomic levels of control in the basal ganglia. One gets a glimpse of this assumption in this case, in which the functional passes into the organic; what the pathologic transformation, in form and fact, must be is left for further interpretation.

The two reels concluding the demonstration visualized the clinical histories of unusual types of sequela of epidemic encephalitis. These films were likewise synchronized.

DISCUSSION

DR. JAMES S. EDLIN: Cinematographic visual education is no longer an experiment. No modern educational institution is minus the facilities for motion picture demonstration. The oral age has given way to the present period in which things must be visualized in order to grasp them more clearly. In medicine, however, such a modern progressive method of education has been slow of adoption. Medical men are far too conservative.

Historically, cinematography dates back to 1877, when the Germans first used it to illustrate the pathology of spinal and nervous ailments. This was followed by studies of orthopedics, laryngology and physiology. The second stage in this work began with the discovery and development of roentgen technic, and the third was the combination of the microscope with the cinema camera.

In 1899, Marie, in France, adapted the cinema to a study of motion within the field of the microscopic lens. Comandon, then a young medical student at the Sorbonne, advanced further and utilized the cinematograph in the newly discovered field of ultramicroscopy. Later, in 1911, Comandon, in conjunction with Lomon of Paris, produced a radiograph cinema showing the skeleton of an entire animal in all of its moving details, even to such small items as the movements of the patella of the knee joint. The thoracic cage moved hurriedly or slowly with the respiration. The heart distinctly pulsated in perfect outline. The liver was seen moving up and down with the diaphragm and was shown clearly in the intestinal mass. Associates of Comandon registered cinematographically the different phases of the phenomenon of phagocytosis, of the trypanosome showing the attachment of the trypanosomes to the white globules, their englobement and their destruction, and also the details of the trypanolysis.

In July, 1908, a London hospital installed a complete cinematographic outfit in the operating room for the recording of interesting surgical technic. In Paris, Dr. Doyen devised special machines to illustrate his course in surgery with cinematographic films. In this country, the earliest use of cinematography appears to have been made by Dr. Walter G. Chase of Boston, who used it in 1905 to record and reproduce an epileptic attack in its entirety. He also used it to depict one rare case of double nystagmus in which the movement of the eyes was clearly shown. In 1913, cinematography was used in the study of embryology and tissue growth by Dr. McWhorter and Dr. Prince, Jr. The object of the authors was twofold: (1) to reproduce the changes in the tissue growth and early development of the embryo and (2) to reproduce for further study such movements as are not readily followed by the eye, for example, the exceedingly slow movements

incident to the growth of tissue and cell divisions. This was accomplished by adapting cinematography with ultramicroscopy.

Cinematography has been made a method of demonstration by the Mayos, Crile, Albee, Douglas and many others. Within the past two years the American College of Surgeons has assisted in the production of several medical and surgical subjects. This is the direct result of conferences between Dr. Franklin H. Martin, Rear Admiral William C. Braisted, M.D., and myself, as president of the Society for Cinematographic Instruction in Medicine and Surgery, at a meeting of the American College in Philadelphia in October, 1921.

Among the pioneers in medical cinematography here are Dr. Weisenburg, Dr. Tilney and Dr. Goodhart. Dr. Tilney and Dr. Goodhart were the first to use "slow motion" photography — "bradykinetic analysis" as they described it — in the study of the deformities of motion in nervous diseases.

No matter how clearly Dr. Goodhart described and analyzed his neurologic cases orally, his description is tremendously enhanced by the addition of clinical reproduction on the film. Even the most acute human eye would fail to detect the fine vermicular waves which he had demonstrated in the case showing both psychogenic and organic elements.

With the development of sound cinematography, we are again utilizing it in medical application. Nearly two years ago and long before the Radio Corporation of America photophone was ready to launch its device on the theatrical market, Dr. Goodhart and I were privileged, through Mr. David Sarnoff, to experiment in recording medical and surgical films. The result of that experiment we saw here.

Having personally had a hand in the development of cinematography in medicine and surgery and having watched it further develop in the hands of others I can see its wonderful educational future with the addition of color and stereoscopy to sound. What a great future for medical education seems to be in store for this method of demonstration I shall ask you to judge from the demonstration.

Book Reviews

MENTAL HYGIENE AND SOCIAL WORK. By PORTER R. LEE and MARION E. KENWORTHY. Price, $1.50. Pp. 309. New York: The Commonwealth Fund, Division of Publications, 1929.

This publication of the Commonwealth Fund consists of two parts: the first describes the work of the Bureau of Children's Guidance during the years 1921 to 1927, and the second, the training for psychiatric social work given by the New York School of Social Work during the same period.

As an introduction to the first part, the authors discuss the peculiar contributions made by a child guidance clinic to the treatment for behavior problems: 1. Such studies of children's problems help substantially to an understanding of the emotional problems which underlie conduct. Nothing is clearer as a result of experience in a child guidance clinic than that human behavior in its pathologic, unsocial and unsatisfying aspects cannot be understood completely without as far-reaching and as scientific a study as is needed for an understanding of physical health and disease. 2. Such studies add substantially to the stock of methods for handling children and to the precision with which the methods can be used, although the methods of treatment are distinctive and less in their inherent character than in the precision with which they are used and the degree of penetration into the situation which they make possible.

The authors follow these preliminary remarks with a description of the philosophy underlying such treatment. Treatment to be efficacious must be directed to the etiologic factors which produce the symptoms. In order to understand the etiologic factors, it is necessary to study the individual presenting the problems from as many angles as possible—psychologic, sociologic and physiologic. For this reason the fourfold study plan—a social, psychologic, physical and psychiatric investigation of the individual, his growth and environmental experiences by a psychiatrist, a physician, a psychologist and a social worker—was developed. The correlation of the results of these studies, the implications from them as to the direction and type of treatment and the great facility by which treatment plans may be put into practice furnish the unique character to a child guidance program.

The most important single factor in the development of the child's personality lies in his relationships with his parents and their attitudes toward him. These parental attitudes are, of course, the result of the parents' own personality problems. The authors discuss these parent-child relationships, describing various rather typical mother and father child relationships which tend to produce maladjustment of the latter. This is followed by a discussion of the manner in which the child's actual experiences—illnesses, habit training, growth experiences (weaning, etc.), the presence of siblings, school, etc.—exert an effect on his personality development, both directly and through their influence on his relationships with his parents.

Throughout this portion of the book the emphasis, both in theory and as deduced from case histories, is placed on the child's need for security and a satisfying relationship with his parents. This is true as far as it goes, but on reading these chapters one gets the impression that it is necessary only to catalog the individual's experiences (whether adult or child) as to their constructive or destructive and satisfying or unsatisfying components and to change the environment to replace those which are destructive and unsatisfying with some which are both constructive and satisfying in order to produce therapeutic results. No account seems to be taken of the many other mechanisms—guilt coming from an incestuous attachment to a parent, etc.—which are of equal if not greater importance. In fact many of the parental maladjustments, which the authors explain on the basis of lack of emotional satisfaction and would treat by supplying these lacks, might be explained on an entirely different basis, for which such treatment would be at best palliative, if not definitely destructive. It is true that the basis for an unresolved attachment to a parent—with the guilt and distress which arise from this attachment—probably

lies in the attempt of the parent to satisfy his own maladjustments at the expense of the child, but the possibility of changing the symptoms arising from such an attachment by supplying a more constructive type of parent substitute becomes distinctly unfeasible very early in the child's life, at the time when the environment becomes internalized and the individual reacts not to his environment but to his environment as he sees it in the light of his past experiences.

Such an explanation of the cause of the behavior of many of the children that come to a child guidance clinic and the attitudes of the parents and the treatment implications which arise out of it makes the reviewer wonder for whom this book is intended. It presents a philosophy that was undoubtedly the best at the period during which the Bureau of Children's Guidance operated and was immeasurably superior to that of many agencies dealing with children during the early years of the Bureau's existence. Increasing experience with children's problems, however, makes it doubtful if the authors really agree at present with the point of view presented in this book.

For this reason the book seems undesirable for lay consumption and for the perusal of physicians, social workers, student psychiatrists or other professional groups interested but not conversant with child guidance practice. For the trained psychiatrist it presents a point of view that is perhaps only of historical interest. A similar criticism may be applied to the chapter on treatment. In many of the problems met with in child guidance practice such superficial treatment may be palliative to the point of removing the disturbing behavior for which the child was referred. They certainly would have little effect on the more serious personality problems. Throughout, the tendency in treatment of parents seems to have been to develop a relationship with the parent whereby the latter becomes dependent on the Bureau and can then accept the suggestions of the Bureau as to the best methods of handling the child. Such a relationship does not help the parent to work out his own personality problems to the point where he no longer needs the emotional dependence for guiding his life. This may help the child in some cases, but leaves the real problems of the parents untouched and therefore is not real preventive therapy.

The first section of the book provides interesting reading for the person who has had actual experience in therapeutic work with problem children, but cannot be recommended for general lay or professional consumption. The second part of the book describes the training given to psychiatric social workers at the New York School of Social Work. The various courses are outlined and field work is discussed. Most important of all a chapter is devoted to considering the personality of the individual worker, the manner in which his own problems interfere with his ability to incorporate psychiatric philosophy into his own thinking, and as a result interfere with his case work, and the pedagogic problems which the personality problems of the students raise. This part should be of interest and value to all those engaged in training or supervising students in social work.

DER SCHLAF. MIT BEITRÄGEN VON C. VON ECONOMO, H. MILITOR, E. P. PICK, O. PÖTZL und A. STRASSER. Herausgegeben von D. Sarason. Price, 5.50 marks. Pp. 107. Munich: J. F. Lehmanns, 1929.

Sleep as a biologic and physiologic phenomenon has attracted much interest among investigators in the last decade. The monograph under review is a complete presentation of the views on sleep of the Viennese school. The editor, Dr. Sarason, in a brief introductory article, gives the general biophilosophic premises to the problem and points out the practical value of better knowledge of this important function from a clinical and especially from a therapeutic standpoint. The monograph is arranged in three parts: Biology and the Clinical Aspect of Sleep; Pharmacology of Sleep-Inducing Drugs, and the Hydrotherapeutic Treatment of Sleeplessness. In the first article on sleep as a problem of biodynamics, O. Pötzl considers sleep as a general biologic phenomenon and discusses the correlatives of this phenomenon in the physiology of protozoa, plants and lower and higher animals. The alternation between the anabolic and catabolic processes in the protoplasm

is the foundation of sleep as a biologic phenomenon. The aspect (morphology) of this phenomenon and its mechanism follows the evolution of protoplasm from the simplest to the highest organizations. Periodic modification of the statics (Haltung) and coincident periodic shifting of the functions — the two principal traits of sleep in higher animals — can be traced as far back as to the lower plants. In the lower forms of organization of protoplasm the biologic correlative of sleep is a diffuse phenomenon, a simple physicochemical reaction entirely and closely bound to the changes of the medium into which the lower organism is placed; only with differentiation of the nervous system comes differentiation of the function of sleep regulation. In higher animals sleep is a function under command of central innervation.

In the second article, O. Pötzl studies sleep as a psychic problem. The influence of another Viennese master is felt in the author's approach to this subject. Freudian concepts of the subconscious activity of the mind, the rôle of dreams, are considered on a strictly biologic basis. The author points out that both phenomenologic and psychoanalytical studies meet together in bringing forward the view that sleep is a positive, active function, thus establishing the link between the psychologic and psychoanalytical aspects of sleep, on the one hand, and the problem of cerebral localization on the other. The latter problem is dealt with by C. von Economo in the third article entitled "Sleep as a problem of localization." The author gives first an introductory consideration of the concept of the nervous center in general; he defines the center broadly as an agglomeration of the gray substance, the activity of which is of immediate and primary importance for the presence of a definite function. On the following pages he gives an historical outline of the evolution of ideas on the nervous mechanism of sleep. Clinicopathologic experience with epidemic encephalitis, the observations on Wernicke's encephalitis hemorrhagica superior, Gayet's disease, and tumors of the infundibular region lead the author to the conclusion that in the peduncular region of the midbrain, in the area contiguous to the cephalic end of the sylvian aqueduct between the hypothalamus and oculomotor nuclei, is located a central apparatus regulating sleep. This sleep-regulating center consists probably of two antagonistic components; one sleep-inhibiting, located caudad, and another sleep-promoting, located cephalad. Thus arise two clinical varieties of the syndrome of lesions occurring in this region, one with chorea and insomnia, the other with oculomotor disturbances and excessive sleepiness.

In the fourth article, O. Pötzl discusses the physiology of sleep and speaks of circulatory, respiratory, metabolic and glandular functions and of their modifications in sleep. The clinicobiologic part of the monograph is concluded by the article of O. Pötzl on sleep as a therapeutic problem. The aspect of sleep in various pathologic and borderline conditions, the theoretical foundations for therapeutic methods and the general indications for choosing these methods, when dealing with various forms of sleep disorders, are discussed in an interesting and instructive manner.

The second part of the monograph consists of one article by H. Molitor and E. P. Pike on the pharmacology of sleep-inducing drugs. After a brief historical review of the discovery of the principal drugs, the authors discuss the general properties of sleep-inducing drugs and the old principle of classification of these drugs into narcotics and hypnotics. As H. H. Meyers and his school established, it is not the chemical constitution, but its physicochemical properties, that gives the measure of the narcotic action of a substance. The basic criterion of a narcotic substance is its lipoid solubility. This lipoid theory of narcosis gave the basis for an entirely new physiologic classification of the sleep-inducing drugs. Thus, the Viennese school classifies such substances according to their relationship to the physiologic process of sleep and according to their particular affinity for certain definite zones of the cerebrum into cerebral or cortical hypnotics, and into brain stem or subcortical (thalamic) hypnotics. Typical examples of the first group are bromides paraldehyde, chloral hydrate and alcohol, while typical examples of the second group are the barbituric acid compounds.

The third part of the monograph on the hydrotherapeutic treatment for sleeplessness is dealt with by A. Strasser. This part consists of a study of the

physiologic effect of hydrotherapy. There is a discussion of the technic and an analysis of the clinicotherapeutic indications for treatment in insomnia of different kinds — the insomnia of arteriosclerotics, of neurasthenia, of hysteria and of psychoses. The monograph is published simply and is well put together and printed.

DER AUFBAU DER FUNKTIONEN IN DER HÖRSPHÄRE. By WALTER BÖRNSTEIN. Price, 9.60 marks. Pp. 126. Berlin: S. Karger, 1930.

This interesting monograph is concerned fundamentally with the application of the Gestalt theory to brain physiology. More specifically, the question investigated is whether acoustic stimuli of different sorts go to different parts of the cortical auditory center, and whether different sounds excite specific areas within the auditory centers of the cortex. Börnstein says that neither the auditory centers nor the auditory tracts are differentiated for different sounds; that is, the auditory gyri in the cortex contain no centers for tone qualities (clearness, volume, etc.), nor do they contain centers for pitch.

He emphasizes what he calls the principle of concentric narrowing. In an injury of a part of the auditory cortex (the transverse gyri of one or both hemispheres), the rest of the auditory cortex takes over the function of the whole, but in a diminished way according to a definite principle. The best heard, most important tone range biologically is the least injured. The parts radiating in all directions from this "nucleus" are the most injured. This is the law of concentric narrowing. The principle of auditory function is part of a greater principle, the "law of plasticity." The building up of the auditory sphere is carried out by the formation on the auditory center of a higher sensorimotor level, of speech and music.

The monograph is interestingly written and contains numerous references to clinical material. It takes full cognizance of the previous contributions to the subject. The relation of the higher to the lower auditory functions and the process of dissolution of these functions with the subsequent development of aphasia are discussed in a clear and interesting fashion. The book should prove useful and valuable to neurologists and psychologists.

LES DÉLIRANTS. By RAYMOND MALLET. Price, 12 francs. Pp. 97. Paris: Gaston Doin, 1930.

This book is a typical example of classificatory psychiatry interested in what is accessible for a clinical demonstration, lecture and correlation with the local literature and lines of discussion. It makes of psychiatry too little of a study of the patient and the problem of possible adjustment than a disquisition or the general patterns needed by the routinist in disposing of cases and in teaching. It is from this point of view that the little booklet gives a good picture of present-day French conceptions, a progress from mere symptomatology to an interest in pathogenic theories oriented in the direction of a general pathology. What is a delusional state (délire)? Its material or content? Its organization or construction?

A delusional state is an irreducible element, the starting point of an automatic activity of thought in conflict with voluntary activity, at first as in the obsessed with insight but more and more swayed either by hallucinations and secondary interpretation, without confusion or dementia, or by some dominant topic of revenge or invention, or mysticism; or by interpretations, or passion, etc., hypochondriac or imaginative. The automatism is related to histologic lesions, infectious or toxic (especially tuberculous and syphilitic), acute or chronic, affecting the association systems rather than the nerve centers themselves. The disorder may be constitutional or acquired, degenerative or disharmonious; affective dissociation releases automatism. Neurovegetative and endocrine disorder always involves cenesthesis. The organic lesion is the same as in obsessions, but more developed. The encephalitic hallucinatory psychosis and a case of frontal tumor (Vincent) are offered as organic evidence.

DER KOPFSCHMERZ UND SEINE BEHANDLUNG. By EUGEN POLLAK. Price, 9 marks. Pp. 155. Vienna: Franz Deuticke, 1929.

The monograph is divided into two parts. In part 1 Pollak discusses in a general way the various kinds of headache encountered in every day practice, their pathophysiology, localization, character, intensity and mode of onset. Part 2 consists of sixteen chapters: trauma and headache, headache in expanding cerebral lesions, inflammation of the brain and headache, headache in infectious diseases, in circulatory disturbances (migraine), in endocrine disorders, in the neuroses, due to diseases of the eye, ear, nose (and accessory sinuses) and teeth, trigeminal and occipital neuralgia, muscular headache and headaches produced by therapeutic and other "diagnostic" methods (lumbar puncture, encephalography, etc.). The last chapter is devoted to the symptomatic treatment for headaches the causes of which cannot be determined. The monograph is concluded with a valuable bibliography of seven pages, with references to each type of headache described in the text.

The book is well written but contains nothing that is not already known, and will probably appeal more to the student of medicine and general practitioner than to the neurologist.

MAMMALIAN PHYSIOLOGY. A COURSE OF PRACTICAL EXERCISES. By E. G. T. LIDDELL and SIR CHARLES SHERRINGTON. Pp. 160. Oxford: Clarendon Press, 1929.

This book represents a new edition of Sir Charles Sherrington's excellent manual of mammalian physiology. E. G. T. Liddell has collaborated with Sir Charles Sherrington in the preparation of exercises with which both have had much experience in teaching students. The arrangement of the book and the choice of exercises are excellent. Many of the latter have been revised. One new exercise on the inhibitory action of the cerebellar cortex has been added. The preparations used throughout the manual are decapitate and decerebrate animals, and the entire course consists of twenty-two exercises each of three hours' duration. The directions are clear and precise.

The manual is an excellent laboratory guide, is well illustrated and printed and can be highly recommended to teachers and students. The references for further reading found at the end of many of the exercises are particularly valuable.

A CHALLENGE TO NEURASTHENIA THROUGH A PATIENT'S EYES. By DORIS MARY ARMITAGE. Price, 1 shilling. Pp. 52. London: Williams & Norgate, 1929.

This little book is easy reading and interesting. It sets forth clearly and simply the different ways in which Dr. L. S. Barnes of England, now deceased, met and overcame certain aspects and circumstances which arose during his treatment of neurasthenic patients. He found fear the root of all neurasthenic troubles, and worked tirelessly with his patients until this was overcome, teaching them that lasting cure was to be found only through an intelligent facing of their problems and a grasping of the contradictions of which these consisted. He is quoted as saying, "I am no miracle worker, I teach you to cure yourself." Although this book is written by a layman, it shows clear insight into the subject of neurasthenia, and is a faithful representation of the methods employed by one who knew his subject thoroughly.

DISEASES OF THE BLOOD. By PAUL W. CLOUGH, M.D. Price, $3. Pp. 310. New York: Harper & Brothers, 1929.

This small book gives a clear and concise exposition of the present knowledge of the diseases of the blood. In view of the large number of instances of pernicious anemia with early cord symptoms, many of which come to the attention of the neurologist first, the discussion of the anemias, particularly pernicious anemia, should be of interest to neurologists. The illustrations are excellent.